EXPOSURE ASSESSMENT -- REFERENCE INFO

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The F-16 Aircraft and Hydrazine— An Industrial Hygiene Perspective

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ABSTRACT

This paper describes the USAF program for controlling potential exposures to hydrazine as it is used on the F-16 aircraft. The evaluation of exposures to hydrazine during various aircraft maintenance activities is described. Cooperation between a defense contractor and the line and medical service of the USAF led to an engineering design concept which emphasizes control of exposure and minimizing the potential of accidental exposure. Recognizing that the risk of an accidental exposure will never be reduced to zero, the USAF Medical Service has implemented a comprehensive program of medical surveillance and health education directed towards the work force responsible for maintenance of the F-16 hydrazine system. The paper has crossover interest to non-toxicologists and non-industrial hygienists; it demonstrates the benefit of consulting the medical community early in the development and acquisition of any new system which involves potential exposure to hazardous materials.

THE F-16 AIRCRAFT relies on continuous electric and hydraulic power to maintain the position of flight control surfaces. In certain flight envelopes, the loss of either power will result in loss of flight control within a matter of seconds. Since maintaining flight stability is critical to a successful engine restart or crew ejection, the aircraft has been equipped with an emergency power unit (EPU) which senses disruption in either electric or hydraulic power and initiates a backup power source. A blend of 70% hydrazine and 30% water (H-70) is used to supply energy for the backup system. The fuel is decomposed on a catalyst which produces high temperature gases to drive a generator and a hydraulic pump. While the USAF had considerable experience from the space and missile program in handling hydrazine, the introduction of this toxic material to the flightline presented new and challenging problems to the USAF medical and aircraft maintenance communities. Mindful of the concern for the toxicology of hydrazine (1,2),* and that deployment of the F-16 would increase the USAF population at risk of exposure, the USAF Surgeon General directed the publication of an Air Force Occupational Safety and Health (AFOSH) standard on hydrazine (3).

The Harry G. Armstrong Aerospace Medical Research Laboratory (AAMRL) and the USAF Occupational and Environmental Health Laboratory (OEHL) both had a major role in defining medical support requirements for the F-16 system. AAMRL's toxicology research program developed the data base for identifying safe human exposure and engineering design criteria for hydrazine before the F-16 was introduced into the field. Figure 1 illustrates, in general, the uses of the toxicology data base for new chemicals used in advanced weapons systems. The OEHL worked with the F-16 Systems Program Office during the full-scale development phase of aircraft testing to insure that medical and industrial hygiene interests were given careful consideration before aircraft deployment. Both AAMRL and the OEHL are components of the Aerospace Medical Division (AMD) which is a division of the Air Force Systems Command.

This paper is intended to have crossover interest to non-toxicologists and non-industrial hygienists. It is an overview of a systematic approach to industrial hygiene. The paper focuses on field experience with use of H-70 on the F-16 as a highly successful example of how and why the medical community should be consulted early in the development and

*Numbers in parentheses designate references at end of paper.

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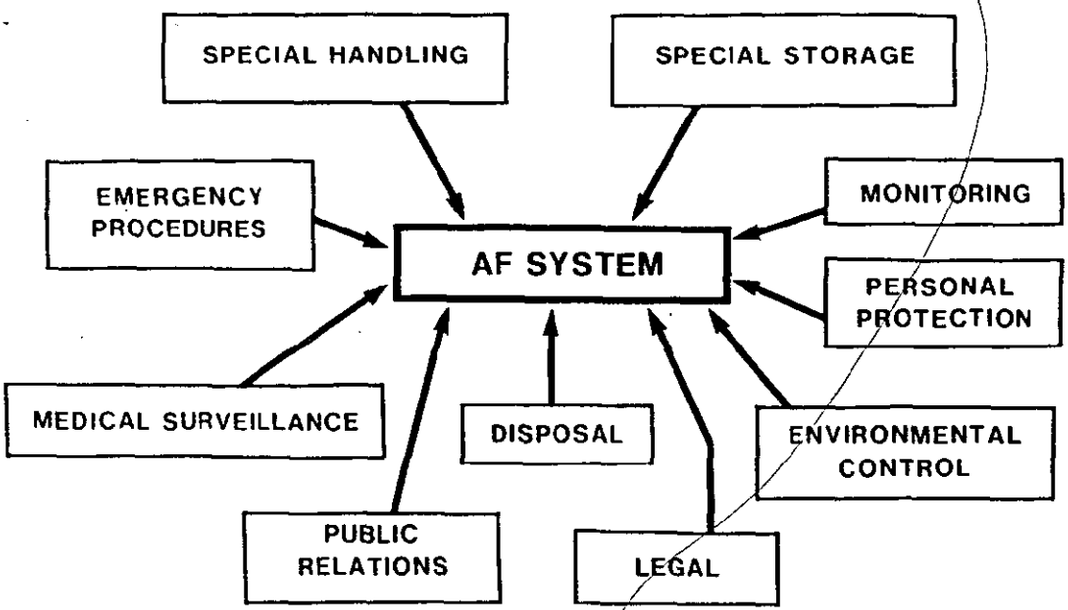

Figure 1. Uses of Chemical Toxicology Technology Base

acquisition of any new system which involves potential exposure to hazardous materials.

HYDRAZINE TOXICOLOGY AND WORKER EXPOSURE CRITERIA - Hydrazine is a widely used industrial chemical. In addition to its use as a propellant by the DOD and NASA, it is used as a blowing agent, a reducing agent, an oxygen scavenger in boiler water treatment, and in the synthesis of various chemicals and drugs. In 1974, it was estimated that 17,000 metric tons of hydrazine were produced in the United States (2). The National Institute for Occupational Safety and Health (NIOSH) estimates that approximately 9,000 workers are potentially exposed to hydrazine (2).

Hydrazine is a clear, oily liquid having an ammonia-like odor. The odor threshold is reported to be 3 to 5 ppm (3). Since individual sensitivity to odor may vary and prolonged exposure can overcome sensory recognition, the odor cannot be relied upon as an indication or warning of overexposure.

Hydrazine is a corrosive compound. Skin contact with the liquid or exposure to high vapor concentrations can cause eye and/or skin irritation. The contact dermatitis can vary from a mild rash to severe burns, depending upon the amount of hydrazine present and the duration of exposure (3).

Hydrazine is readily absorbed through the skin; however, immediate rinsing with water will reduce both the uptake and the chemical burns from skin contact. If allowed to penetrate the skin, the toxic effects will be similar to those described below from inhalation (3).

Contact of the eye with liquid hydrazine or high vapor concentrations can cause temporary or permanent blindness. Contact with the lining of the airways and lungs can cause irritation of the lining or the development of fluid within the lungs (3).

At high doses, hydrazine can cause disruption of normal central nervous system function. The first symptoms may be headaches, dizziness, loss of balance, or nausea and vomiting. If the dose received during overexposure is sufficient, loss of consciousness and respiratory failure may result. Although convulsions have been reported in experimental animals at very high doses of hydrazine, they have not been reported in humans. It should be noted that this is not true for the substituted hydrazines, such as methylhydrazine and dimethylhydrazine, which are potent convulsigenic agents (3).

A primary hazard associated with excessive hydrazine exposure concerns its ability to produce liver damage. This can occur as a mild condition diagnosed only by altered clinical chemistry tests or as severe liver cell death, resulting in normal liver tissue being replaced by scar tissue. In the less severe response, liver function may return to normal when the individual is removed from the exposure situation; whereas in the more severe response, the liver is permanently damaged. The degree of severity is directly proportional to the duration and amount of exposure (3).

There is evidence from animal experiments that hydrazine is capable of inducing respiratory tumors in long-term inhalation studies. A dose-related response was observed in one-year exposures to 1.0 and 5.0 parts per million (at 25°C, 760 Torr). No increased incidence of tumors was observed at 0.25 and 0.05 ppm (4).

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Hydrazine has exhibited a teratogenic effect in rats causing embryo death at doses approaching those causing overt maternal toxicity. The data indicate the 0.1 ppm is a no-risk level for pregnant women and their fetuses. However, the embryo would be at greater risk than adults in the event of an accidental spill leading to a short-term, high-level exposure either by inhalation or percutaneous absorption (5).

Hydrazine permissible occupational exposure limits for Air Force applications are specified in AFOSH Standard 161-13 (3). The maximum eight hour time weighted average (TWA) airborne concentration of hydrazine to which personnel may be exposed is 0.10 ppm or 0.13 mg/m^3. At this concentration, nearly all workers may be repeatedly exposed, day-after-day, without adverse effect.

Excursions to a concentration of 0.30 ppm or 0.39 mg/m^3 are permitted providing that the TWA is not exceeded during the workday. This is the concentration to which workers can be exposed continuously for a short period of time without ill effects. Excursion should be measured over 15 minute periods.

Since skin absorption of hydrazine may contribute to the overall exposure, AFOSH Standard 161-13 specifies that liquid hydrazine should never be allowed to come into contact with unprotected areas of the body.

SYSTEM DESIGN OBJECTIVES - The Occupational Safety and Health Act of 1970 formalized, in legislation, what had been considered by many engineers to be "good engineering practice." Within the engineering design community, the Act forced recognition of "personnel exposure control" as an essential element in total system design. The continuous electric and hydraulic power requirements of the F-16 prompted serious consideration of a hydrazine (H-70) powered emergency power system but raised many questions about the wisdom of introducing a toxic chemical into the flightline environment. Concurrent with the design decision to incorporate a hydrazine system on the F-16 was a commitment to identify system design objectives which would:

- provide hardware and support equipment designed to preclude exposure to liquid or vapor through a closed system approach;
- provide a warning system to positively alert personnel to possible exposure situations; and
- provide personnel with qualified personal protective equipment, specific task-oriented technical data, and a comprehensive occupational health program.

The F-16 EPU was designed as a totally closed system to minimize the risk of personal exposure. During normal operations, the liquid hydrazine tank is isolated from the pressure tank. Whenever the system is used, there is a positive indication at the flight console. The fuel tank remains pressurized until maintenance is performed. A positive indication in the form of a pressure gauge has been included in the system to show that the H-70 tank is pressurized and as a warning to maintenance personnel. Flightline servicing of a used EPU involves depressurization of the system, purging residual H-70 contained in the wet-side plumbing through the catalyst bed, and replacing the used H-70 tank.

All EPU maintenance is accomplished using specific instructions which describe the tasks and which have been validated by industrial hygiene measurements of airborne hydrazine concentrations. To service a pressurized system, personnel are required to wear gloves, apron, and a face shield to protect them from accidental release of a liquid stream. Depressurization is accomplished through a scrubbing device designed to neutralize any possible hydrazine vapor that may have wetted the interior walls of the H-70 tank as the plunger traveled along the tank.

All quick-disconnect fittings on the wet side were selected for their high integrity and small interior volume to minimize liquid release. As an extra measure, disconnect is accomplished with a wetted rag wrapped around the fitting to trap any small liquid release. The rag is neutralized in the scrubbing liquid to further reduce exposure risk. The final steps in flightline servicing of the H-70 system involve purging of residual H-70 in the downstream plumbing and removal of the H-70 tank.

The closed-system concept is carried to non-flightline servicing of the H-70 tanks as well. The tanks are transported in specially designed containers equipped with a color indicator to give positive warning that a leak of H-70 may have occurred in the container. The tanks are serviced by technicians wearing clothing similar to that used by flightline maintenance personnel since refilling involves pressurization of an H-70 drum.

During system development, USAF bioenvironmental engineers worked with contractor industrial hygienists and design engineers to measure exposures and validate both the equipment design and maintenance procedures. Where exposures were found to approach levels greater than half the acceptable exposure criteria, modifications to both equipment and procedures were accomplished. Exposure measurements have shown that hydrazine can be maintained at an order of magnitude below the exposure criteria. An example of hydrazine breathing zone concentrations measured during F-16 EPU maintenance tasks is given in Table 1 (6).

No amount of preparation will reduce exposure risk to zero. Training of personnel in the proper use of equipment and procedures is a necessary ingredient to achieving low exposures. Videotape and slide/tape visual aids are used for initial and periodic training of all maintenance personnel. In addition, a comprehensive occupational health program to monitor the exposures of potentially exposed personnel and provide annual physical examinations has been introduced.

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Table 1. Hydrazine Breathing Zone Concentrations Measured During F-16 EPU Maintenance Tasks

TASK DESCRIPTION	WORKER DESIGNATION	TASK AVERAGE CONCENTRATION (mg/m^3)	CALCULATED 15 MIN EXCURSION CONCENTRATION (mg/m^3)[a,c]	CALCULATED 8 HR TWA CONCENTRATION[d] (mg/m^3)
A. Servicing Facility Tasks				
1. Drum Change Out[b]	A	0.014	0.014[a]	0.0003
	B	0.005	0.005[a]	0.0001
	C	0.011	0.011	0.0002
2. Fuel Tank Fill (1st Test)	A	0.001	0.007	0.0002
	B	0.003	0.016	0.0005
	C	0.003	0.018	0.0006
3. Fuel Tank Top Off	A	0.092	0.29	0.009
	B	0.021	0.066	0.002
	C	0.066	0.21	0.007
4. Fuel Tank Defueling	A	0.018	0.021	0.0006
	B	0.017	0.019	0.0006
	C	0.025	0.028	0.0009
5. Fuel Tank Fill (2nd Test)	A	0.018	0.081	0.003
	B	0.012	0.054	0.002
	C	0.019	0.087	0.003
B. Flight Line Tasks				
1. Fuel Tank Depressurization	A	0.011	0.014	0.0004
	B	0.009	0.012	0.0004
2. Fuel Line Purge	A	0.005	0.013	0.0004
	B	0.003	0.007	0.0002
3. Poppet Valve Refurbishment	A	0.041	0.054	0.002
	B	0.004	0.005	0.0002
4. Fuel Tank Replacement	A	0.018	0.025	0.001
	B	0.008	0.010	0.0004

a These calculated excursion values were taken to be the same as the task average concentration because the task duration was less than 15 minutes. This is a conservative interpretation of the data.
b There was no worker exposure during this task since each worker wore self contained breathing equipment; the results are for breathing zone samples taken on the outside of respiratory protective gear.
c Assumes all exposure during task occurred during a single 15 minute period.
d Assumes total 8 hr duty day exposure to hydrazine occurred during performance of task.

DISCUSSION

The integration of occupational and environmental health guidance and design criteria early in the F-16 development and test phases significantly enhanced operational utility and supportability. This experience clearly indicates that early involvement of the medical and industrial hygiene communities in hardware design and development of systems using toxic substances is absolutely essential if the technology is to be supportable in the operational environment. As the state-of-the-art in aircraft design moves beyond F-16 capabilities, the requirement for high-energy, quick-response power will demand the use of new fuel and chemical systems. The lessons learned during the development of the F-16 can be of great value in designing occupationally and environmentally safe systems using new fuels and chemicals.

To help promote this approach, the Department of Defense System Safety Program has incorporated an occupational health hazard assessment task to permit program managers a formal mechanism for obtaining health related data upon which to base trade-off decisions among candidate chemicals, system performance, and medical support requirements (7).

SUMMARY

Through the combined efforts of the aircraft manufacturer, the F-16 Systems Program Office, and the USAF Medical Service, measures have been taken to reduce the potential risk of exposure to hydrazine during maintenance of the F-16 aircraft. The use of a closed-system design objective has reduced exposures during routine EPU servicing to levels more than an order of magnitude below the occupational exposure limits for hydrazine. A comprehensive

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program of medical surveillance and worker education has been implemented to further reduce exposure risk.

REFERENCES

1. American Conference of Governmental Industrial Hygienists. Documentation of the Threshold Limit Values for Substances in Workroom Air, 4th Edition, 1980.
2. National Institute for Occupational Safety and Health, Criteria for a recommended standard . . . occupational exposure to hydrazines. DHEW (NIOSH) Publication number 78-172, 1978.
3. HQ USAF Surgeon General, Air Force Occupational Safety and Health Standards on Hydrazine. AFOSH Standard 161-13, Washington DC, 1979.
4. MacEwen, J.D., E.H. Vernot, C.C. Haun, E.R. Kinkead, and A. Hall III, "Chronic Inhalation Toxicity of Hydrazine: Oncogenic Effects," AFAMRL-TR-81-56, Jun 81 (AD A101 847).
5. Keller, W.C., C.T. Olson, K.C. Back, and C.L. Gaworski, "Evaluation of the Embryotoxicity of Hydrazine in Rats," AFAMRL-TR-82-29, Aug 82 (AD A119 706).
6. Martone, J.A., "The Initial Industrial Hygiene Evaluation of F-16 Emergency Power Unit Maintenance Tasks in USAFE," USAF Hospital, Wiesbaden, Technical Report EHL(W) 82-09, May 1982.
7. Department of Defense, System Safety Program Requirements, MIL-STD-882B, Washington, D.C., 30 March 1984.

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True orofacial dyskinesia secondary to chronic antihistamine administration has been described by Thach et al.[5] and by Davis.[6] This syndrome is clinically indistinguishable from tardive dyskinesia, which generally results from the long-term administration of neuroleptic agents and which may be irreversible.

The fact that antihistamines can cause both dystonic reactions and orofacial dyskinesia is evidence in favor of the hypothesis that antihistamines and anticholinergic agents directly affect catecholaminergic neurones. The experimental work of Farnebo et al.[7] and Coyle and Snyder[8] has suggested such a possibility.

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1. Favis GR: Facial dyskinesia related to antihistamine? N Engl J Med 294:730, 1976
2. Brait KA, Zagerman AJ: Dyskinesias after antihistamine use. N Engl J Med 296:111, 1977
3. Lavenstein BL, Cantor FK: Acute dystonia: an unusual reaction to diphenhydramine. JAMA 236:291, 1976
4. Sovner RD, DiMascio A: Extrapyramidal syndromes and other neurological side-effects of psychotropic drugs, Psychopharmacology — A Generation of Progress. Edited by M Lipton, A DiMascio, K Killam. New York. Raven Press (in press)
5. Thach BT, Chase TN, Bosma JF: Oral facial dyskinesia associated with prolonged use of antihistaminic decongestants. N Engl J Med 293:486-488, 1975
6. Davis WA II: Dyskinesia associated with chronic antihistamine use. N Engl J Med 294:113, 1976
7. Farnebo L-O, Fuxe K, Hamburger B, et al: Effect of some antiparkinson drugs on catecholamine neurones. J Pharm Pharmacol 22:733-737, 1970
8. Coyle JT, Snyder SH: Antiparkinsonian drugs: inhibition of dopamine uptake in the corpus striatum as a possible mechanism of action. Science 166:899-901, 1969

HEPATIC VISUALIZATION AFTER ^{131}I IN PATIENTS WITH THYROID CARCINOMA (CONT.)

To the Editor: The letter of Maayan et al. (Maayan ML, Eisenberg J, Lopez EM, et al: Hepatic visualization after ^{131}I in patients with thyroid carcinoma. N Engl J Med 295:1258, 1976) describes hepatic visualization after large doses of ^{131}I had been given for whole-body scanning to patients with functioning thyroid lobes. They conclude that the ^{131}I-labeled thyroid hormone that had been produced endogenously was accumulated by the liver in a physiologic fashion. We agree with that as a general conclusion.

However, in an experience of more than 150 whole-body scans using ^{131}I to search for metastatic thyroid carcinoma, we have also seen functioning carcinoma in the projection of the liver; eight patients had metastases in the liver, rib, iliac crest or adjacent lymph nodes. The focal nature of the deposits, their localization on scanning in the lateral projection, and radiographs showing skeletal involvement led to a proper diagnostic conclusion in several cases. However, in others one could not be certain with use of these criteria. A clear-cut difference between physiologic hepatic accumulation of ^{131}I-labeled hormone and ^{131}I uptake by metastatic thyroid tumor was possible by analysis of serial, collimated scintillation counting for ^{131}I over the residual thyroid lobe, cardiac blood pool, stomach bed, known functioning metastases and the right upper quadrant of the abdomen (liver). Uptake of ^{131}I by metastatic thyroid carcinoma occurred early, with a time sequence that was similar to the uptake by the thyroid lobe or known metastases. Physiologic accumulation by the liver occurred later, after ^{131}I labeling of thyroid hormone and its release into the circulation had taken place. The lag for physiologic hepatic accumulation was 12 to 24 hours at least.

Comparative serial, focal, collimated scintillation counting over the liver or elsewhere (such as the left upper quadrant to assess metastasis, in contrast to physiologic gastric activity, which rises and falls rapidly in correlation with blood-pool activity) may be useful in differentiating functional metastases and physiologic activity in whole-body ^{131}I scans.

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CHOROIDAL MELANOMA: POSSIBLE EXPOSURE TO INDUSTRIAL TOXINS

To the Editor: We have documented two cases of choroidal melanoma and one case of squamous-cell carcinoma of the conjunctiva, occurring over three years (1971-74) in a population of chemical workers at a plant in the Ohio Valley region. The chemical company involved supplied data, unreviewed by ourselves, stating that only these three cases had occurred over a longer (1956-74) period. They noted that the total age-adjusted incidence of all forms of eye cancer in this population over the longer period was 0.5; this figure would represent a sixfold excess of observed over expected cases and would be statistically significant ($P = 0.023$).[1] Choroidal melanoma is an uncommon human neoplasm, with an age-adjusted annual incidence of six per one million population; from our available data, the total approximate expected incidence in this population during the 1956-74 period is 0.12 cases. Histopathological examination revealed one tumor to be a choroidal melanoma of a mixed cell type (Callender classification). This patient has died of generalized metastases from this lesion. The second tumor was also a choroidal melanoma, of the spindle B type; this patient is alive and has shown no recurrences or metastases.

Detailed work histories for both cases were provided by the employer, who brought these cases to our attention. Although these histories show no known common exposure, the chemical plant uses three substances that have been classified as possible human carcinogens by the American Conference of Governmental Industrial Hygienists: dimethylsulfate, hydrazine, and 4,4′-methylene dianiline. In the first and fatal case, the worker was exposed to hydrazine in a 25 per cent solution of water for six years; in the second case, the worker was exposed to dimethylsulfate for six years.

Although an uncommon tumor, malignant melanoma is the leading primary intraocular tumor. The overall mortality for these tumors is 29 per cent at five years and 40 per cent at 10 years,[2] although overall mortality has been stated to be as high as 65 per cent for large or cytologically malignant tumors.[3] The etiology and pathogenesis of these neoplasms is not known. It has long been suspected that pre-existing choroidal nevi may undergo malignant change, although the evidence for this hypothesis is presumptive.[4] The nature of the carcinogenic insult that could convert a benign nevus or uveal melanocytes into a neoplastic lesion is not known. In cutaneous melanomas, there is a well established relation between the incidence of these lesions and environmental exposure to sunlight.[5] The incidence of choroidal melanoma shows no such relation; a recent study showed no variance in the incidence of choroidal melanoma with latitude, as has been demonstrated for cutaneous melanoma.[6] A recent report linked a polychlorinated biphenyl (Arochlor 1254) with a statistically significant increase in the rate of cutaneous malignant melanoma in workers exposed to this agent.[7] In addition, there have been two reports of intraocular tumors induced in laboratory animals by chemical agents. Benson reported intraocular tumor formation in rats after oral administration of ethionine and N-2-fluorencylacetamide.[8] Patz produced fibrosarcomas of the choroid by intraocular injection of methylcholanthrene.[9]

The possible role of chemical agents in the etiology of human choroidal melanomas requries further investigation. Detailed occupational histories should be obtained in all cases.

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1. National Cancer Institute: Third National Cancer Survey, Incidence data. March, 1975
2. Paul EV, Parnell BL, Fraker M: Prognosis of malignant melanomas of the choroid and ciliary body. Int Ophthalmol Clin 2:387, 1962
3. McLean IW, Foster WD, Zimmerman LE: Prognostic factors in small malignant melanomas of the choroid and ciliary body. Arch Ophthalmol 95:48, 1977
4. Naumann G, Yanoff M, Zimmerman LE: Histogenesis of malignant melanomas of the uvea. Arch Opthalmol 76:784, 1966
5. Elwood JM, Lee LA, Walter SD, et al: Relationship of melanoma and other skin cancer mortality to latitude and ultraviolet radiation in the United States and Canada. Int J Epidemiol 3:325, 1974

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6. Scotto J, Fraumeni JF, Lee JH: Melanomas of the eye and other noncutaneous sites. J Natl Cancer Inst 56:489, 1976
7. Bahn AK, Rosenwaike I, Herrmann N, et al: Melanoma after exposure to PCB's. N Engl J Med 295:450, 1976
8. Benson WR: Intraocular tumor after ethionine and N-2-fluorenylacetamide. Arch Pathol 73:62, 1962
9. Patz A, Wolff LB, Rogers SW: Experimental production of ocular tumors. Am J Ophthalmol 48:98, 1959

AMYLASE-CREATININE CLEARANCE RATIO IN PANCREATITIS

To the Editor: We should like to comment on the recent paper of Johnson et al. (N Engl J Med 295:1214, 1976). The authors present evidence that in acute pancreatitis a renal mechanism (some "tubular-dysfunction factor") is responsible for the enhancement of the amylase-to-creatinine clearance ratio (C_{am}/C_{cr} ratio) rather than an isoamylase abnormality. They state that there is no available information whether this "factor" functions in conditions other than acute pancreatitis.

Earlier reports from several authors and recent findings of our groups have case doubt on the diagnostic value of the C_{am}/C_{cr} ratio in differentiating acute pancreatitis from other disorders. Elevated C_{am}/C_{cr} ratios were found in patients with "acute illness other than pancreatitis,"[1] burns and ketoacidosis,[2] renal insufficiency,[3,4] acute duodenal perforation[7] and after thoracic operations (after thoracic operations also, an increased beta-2 microglobulin clearance was found, providing more evidence that it is the same mechanism that acts upon an enhancement of the C_{am}/C_{cr} ratios in this condition and in an acute pancreatitis).[8] On the other hand, in two independently performed clinical trials we found nonelevated C_{am}/C_{cr} ratios in 10 out of 33 (Göttingen) and 19 out of 46 (Marburg) patients with an established diagnosis of acute pancreatitis during the acute phase of the illness.[5] This means that in our experience, which is in contrast to a recent editorial,[9] a normal C_{am}/C_{cr} ratio does not exclude acute pancreatitis. Thus, the "tubular-dysfunction factor" seems indeed to function in conditions other than acute pancreatitis, and — moreover — seems not to be present in a considerable number of patients with this disease.

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1. Levitt MD, Rapoport M, Cooperband S: The renal clearance of amylase in renal insufficiency, acute pancreatitis, and macroamylasemia. Ann Intern Med 71:919-925, 1969
2. Levine RI, Glauser FL, Berk JE: Enhancement of the amylase-creatinine clearance ratio in disorders other than acute pancreatitis. N Engl J Med 292:329-332, 1975
3. Morton WJ, Tedesco FJ, Harter HR, et al: Serum amylase determinations and amylase to creatinine clearance ratios in patients with chronic renal insufficiency. Gastroenterology 71:594-598, 1976
4. Pederson EB, Brock A, Kornerup HJ: Serum amylase activity and renal amylase activity clearance in patients with severely impaired renal function and in patients treated with renal allotransplantation. Scand J Clin Lab Invest 36:137-140, 1976
5. Bode JC, Bindrich D, Dürr HK: The frequency of macroamylasemia and the diagnostic value of the ratio amylase clearance/creatinine clearance in patients with elevated serum amylase levels. Scand J Gastroenterol [Suppl] 41:74, 1976
6. Lankisch PG, Koop H, Otto J, et al: Specificity of increased amylase to creatinine clearance ratio in acute pancreatitis. Digestion (in press)
7. Berger GMB, Cowlin J, Turner TJ: Amylase:creatinine clearance ratio and urinary excretion of lysozyme in acute pancreatitis and acute duodenal perforation. S Afr Med J 50:1559-1561, 1976
8. Jacobson G: Amylase-creatinine clearance ratio in pancreatitis. N Engl J Med 292:923, 1975
9. Warshaw AL: The kidney and changes in amylase clearance. Gastroenterology 71:702-704, 1976

The above letter was referred to the authors of the article in question, two of whom offer the following reply:

To the Editor. As noted in reference 1 of the letter of Dürr et al., we agree with the contention that tubular dysfunction resulting in an elevated C_{am}/C_{cr} ratio is not entirely specific for acute pancreatitis. So far as the sensitivity of this measurement is concerned, it is our experience that patients with severe acute pancreatitis practically always have an elevated C_{am}/C_{cr} ratio. Patients with what appears to be mild acute pancreatitis occasionally have a normal clearance ratio. However, in such patients, it is seldom possible to document objectively the presence or absence of pancreatitis by some independent method, and it is therefore difficult to determine how often pancreatitis is associated with a normal C_{am}/C_{cr} ratio.

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HUMAN VS. CANINE FOOD

To the Editor: Contrary to Mr. Greenberg's feelings, I doubt very much if it is the failure of the American food industry "to provide humans with a product that approximates the cost and nutritional virtue of many dog foods" (N Engl J Med 295:1487, 1976).

Dog food costs 30 cents a pound because it is manufactured from a limited number of ingredients, in a limited number of forms, and is marketed in a limited number of ways. You won't find it in the frozen-food section of your local supermarket, and Boston has yet to open its first dog-food delicatessen.

The food-processing industry has not "denied" its technologic capacity to the production of human food. That it has not given us a "socially acceptable product nutritionally similar to dog food" is a credit to the profession. (Wom)man is a social animal, and food in many ways defines who and what we are.

During the six weeks from Thanksgiving to New Year's Day our family participated, as most Americans did, in a virtual gastronomic orgy. Food and drink defined our religious beliefs and our social status, facilitated celebration, rewarded the children and brought friends and neighbors together. It gave pleasure, joy, happiness and generated feelings and remembrances of the past. It became symbol, ritual, security, confidence, relief, love and reassurance.

I agree; $1.30 or so a pound for a breakfast product that is nutritionally skimpy is out of proportion. But before I took the food technologist to task I would want to know what part of that cost is represented by excessive marketing costs such as advertising, packaging and extensive and expensive merchandising technics.

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To the Editor: I wholeheartedly concur with Mr. Daniel S. Greenberg's suggestion, in "Dog Food, People Food and Other Matters," that the food industry prepare and market a basic food preparation that will compare with dog food in nutritional value at minimal cost. It would be of particular value to give to improvident families who have one or more members accustomed to trading their food stamps for alcohol, and leaving the children without proper food. The basic food would be less negotiable and easily available to the more dependent members of the family.

Incidentally, such a food does exist, though, to my knowledge, it is not marketed by the food industry. Pemmican was developed by North American Indians as a continuing fine source of all necessary nutrients. It is palatable and can be consumed over long periods without boredom or distaste. I know, since I lived on it as a ski trooper during World War II.

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FUNDAMENTAL AND APPLIED TOXICOLOGY 5, 1050–1064 (1985)

Long-Term Inhalation Toxicity of Hydrazine[1]

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**University of California, Irvine, P.O. Box 31009, Dayton, Ohio 45431; †Naval Medical Research Institute/ Toxicology Detachment, Bldg. 433, Area B, Wright-Patterson Air Force Base, Ohio 45433; ‡Huntingdon Research Centre, Huntingdon, PE186ES Cambs, England; §Physiological Research Laboratories, 1500 Northdale Boulevard, Minneapolis, Minnesota 55433; ‖California Veterinary Diagnostics Inc., 3911 West Capital Avenue, West Sacramento, California 95619; **Primate Research Institute, New Mexico State University, P.O. Box 1027, Holloman Air Force Base, New Mexico 88330; ††U.S. Army Institute of Surgical Research, Ft. Sam Houston, San Antonio, Texas 78234; and ‡‡Dow Chemical, U.S.A., Midland, Michigan 48640*

Long-Term Inhalation Toxicity of Hydrazine. VERNOT, E. H., MACEWEN, J. D., BRUNER, R. H., HAUN, C. C., KINKEAD, E. R., PRENTICE, D. E., HALL, A., III, SCHMIDT, R. E., EASON, R. L., HUBBARD, G. B., AND YOUNG, J. T. (1985). *Fundam. Appl. Toxicol.* 5, 1050–1064. Year-long intermittent exposures of rats, mice, hamsters, and dogs to hydrazine were conducted using concentrations of 0.05, 0.25, 1.0, and 5.0 ppm. Rats were held 18 months postexposure; hamsters, 1 year postexposure; mice, 15 months postexposure; and dogs, 38 months postexposure. Male and female rats exhibited dose-dependent incidences of benign nasal adenomatous polyps and smaller numbers of malignant nasal epithelial tumors after 1 year of exposure to hydrazine and 18 months postexposure holding. Nasal tumors were often associated with chronic irritation and were most frequent in male rats, with an incidence of greater than 50% in the highest exposure group. Hamsters exposed to 0.25-ppm and higher concentrations showed pathologic changes characteristic of degenerative disease, including amyloidosis. After exposure to 5.0 ppm hydrazine, hamsters developed a 10% incidence of benign nasal polyps compared to 0.5% in controls. Small numbers of colon neoplasms and thyroid parafollicular cell adenomas were found in hamsters, but only in the highest concentrations tested. Lung adenomas appeared to be marginally increased in mice exposed to 1.0 ppm hydrazine, the highest concentration tested in this species. No consistent clinical or pathological effects were seen in dogs during or after exposure to hydrazine at any concentration. Using amyloidosis as a criterion, a no-effect level was not achieved in hamsters. In rats, there appeared to be a marginal production of nasal tumors at 0.05 ppm, while mice showed no effects at 0.25 ppm. This study has demonstrated that the nasal respiratory epithelia of rats and hamsters are the most sensitive tissues to the tumorigenic action of hydrazine following inhalation exposures. This is similar to the reaction of rats to formaldehyde, another highly reactive water-soluble compound. © 1985 Society of Toxicology.

Hydrazine (N_2H_4) is a highly reactive reducing agent which is widely used as an intermediate in organic synthesis and, either singly or in combination with other hydrazines, as a missile propellant. An important and increasing use of hydrazine is that of a boiler feed water additive as an oxygen scavenger. Clark *et al.* (1968) provided a detailed review of the toxicology and pharmacology of propellant hydrazines. The acute toxicity of hydrazine is characterized by central nervous system effects, usually convulsive, and by renal and liver lesions (Witkin, 1956; Patrick and Back, 1965).

Interest in the oncogenicity of hydrazine was initially aroused by findings that the antitubercular drug isonicotinic acid hydrazide

[1] The work reported here was performed under U.S. Air Force Contract F33615-80-C-0512. The report is identified as AFAMRL-TR-81-56.

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(INH) induced lung adenomas, leukemias, and lymphosarcomas in mice after intraperitoneal administration (Juhasz *et al.*, 1963). Feeding INH to mice at a concentration of 0.01 to 0.25% in the diet led to the development of pulmonary tumors with dose-dependent incidences (Mori *et al.*, 1960). Similar results were found in various strains of mice by Biancifiori and Ribacchi (1962), Biancifiori *et al.* (1963a,b), Toth and Shubik (1966), Kelly *et al.* (1969), Toth and Toth (1970), and Jones *et al.* (1971). Biancifiori *et al.* (1964) investigated the induction of pulmonary tumors and hepatomas in mice by INH and its putative metabolites, hydrazine (as the sulfate) and isonicotinic acid. Isonicotinic acid had little or no effect on tumor incidence, whereas equimolar concentrations of INH and hydrazine sulfate induced roughly the same incidence of lung tumors. Administration of hydrazine sulfate, but not of INH, led to an increase in hepatomas. Induction of lung tumors in mice by hydrazine, usually as the sulfate, has been repeatedly shown by a large number of investigators (Roe *et al.*, 1967; Toth, 1969, 1971; Biancifiori *et al.*, 1963a,b, 1964; Biancifiori and Ribacchi, 1962; Kelly *et al.*, 1969). Hepatomas and hepatocarcinomas have been observed in three strains of mice treated orally with hydrazine sulfate (Biancifiori, 1970a,b,; Biancifiori *et al.*, 1964; Severi and Biancifiori, 1968). In contrast to the findings in mice, little or no oncogenic effects have been noted in rats and hamsters after administration of INH (Toth and Toth, 1970; Severi and Biancifiori, 1968, Peacock and Peacock, 1966; Toth and Shubik, 1969).

Severi and Biancifiori (1968) administered daily doses of hydrazine sulfate intragastrically to male and female rats for 68 weeks. Lung tumors (adenomas and adenocarcinomas) were observed in treated animals of both sexes and hepatic cell carcinomas or spindle cell sarcomas in males. Toth (1972) administered hydrazine sulfate orally to Golden Syrian hamsters and noted no significant increase in the number of tumors produced.

Wade *et al.* (1981) tested hydrazine in the *Salmonella typhimurium* assay and found it to be weakly positive in the two strains used. Rogers and Back (1981) found that hydrazine induced thymidine resistance in the mouse lymphoma cell assay but was not mutagenically active in ouabain, thioguanine, and cytosine arabinoside systems. Herbold and Röhrborn (1977) reviewed results of different tests for a number of compounds including hydrazine. Hydrazine showed mutagenic properties in the *Salmonella* microsome test and host-mediated assay.

Although workers have had possible exposures to hydrazine vapor for many years and in larger numbers since World War II, there have been no reported cases of hydrazine-induced cancer in humans. The only known epidemiologic study of hydrazine workers reported to date is an ongoing study of a major hydrazine manufacturer (Wald *et al.*, 1984). This study of 427 workmen traced 406 through 1982, of whom 49 had died, 12 from cancers. Both the numbers of deaths and numbers of cancers found for this group matched the expected ratios for English workmen for that period.

In our laboratory, 6-month exposures of CF1 mice to 1.0 and 5.0 ppm hydrazine intermittently and 0.2 and 1.0 ppm continuously (MacEwen *et al.*, 1974) had shown significant induction of pulmonary alveolargenic carcinomas. The study reported here was planned as a follow-up to provide more information on the effects of long-term inhalation exposure of multiple species to hydrazine. This study was designed to expose male and female rats, female mice, male hamsters, and dogs of both sexes to low levels of hydrazine for 1 year, followed by lifetime postexposure holding of rodents for oncogenic evaluation. An exposure period of 1 year was chosen as being representative of the limited period of occupational exposure for career Air Force personnel.

METHODS

Test compound. The anhydrous hydrazine[3] used in this study was analyzed using gas chromatography/mass spec-

[3] 97% pure, Matheson Coleman and Bell, Norwood, Ohio.

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trometry and found to contain 99.8% hydrazine and 0.2% water.

Animals. Female C57BL/6 mice,[4] male and female Fischer 344 rats,[5] male Golden Syrian hamsters,[6] and 6-month-old male and female beagle dogs[7] were used in the study. All rodents were 7 weeks of age at start of exposure. Mice and dogs were not exposed to 5.0 ppm hydrazine because previous experiments (Haun and Kinkead, 1973) had shown this concentration to be lethal to large proportions of these species. The numbers of rodents were chosen to increase sensitivity of tumor detection to the maximum consistent with acceptable animal loading in the chambers. Dogs were included in the study to provide indices of clinical effects mainly from analyses of blood. The first group of mice placed in the 1.0-ppm-hydrazine exposure group was removed from the experiment after an equipment malfunction caused several deaths. A concurrent set of unexposed control mice was established along with the new group of C57BL/6 mice exposed to 1.0 ppm hydrazine.

Exposure and postexposure conditions. Animals were exposed in 840-ft^3 chambers described by Thomas (1965) according to the scheme shown in Table 1. The rodents were housed in stainless-steel cages (25 × 25 × 38 cm). Mice were housed 10 animals per cage, rats 3 per cage, and hamsters 5 per cage. The cages were placed around the perimeter of the chamber with rats at the highest level, followed by hamsters and then mice at the lowest level. Controls were kept in identical cages suspended in racks in the vivarium, a facility separate from the exposure laboratory. Dogs in the exposure chambers were kept in groups separated by sex in 90° sector pens of 4-ft radius. Control dogs were kept in runs at the vivarium. At exposure termination exposed animals were transferred to the vivarium and housed identically to controls for the rest of the experiment.

The exposure concentrations were selected to span a 100-fold range. The 5.0-ppm exposure concentration was selected as an apparent maximum tolerable exposure dose which would produce some biologic response without causing death in hamsters and rats.

The inhalation exposures were conducted on a 6-hr/day, 5-day/week schedule for a 1-year period without exposures on weekends and holidays. The animals were exposed at a slightly negative pressure (725 mm Hg) to prevent contamination of the surrounding laboratories and personnel. The air flow, pressure, relative humidity, and temperature were all controlled automatically. Air flow was maintained at 40 ft^3/min (1.1 m^3/min), relative humidity at 50 ± 10%, and temperature at 22 ± 2°C.

TABLE 1

EXPERIMENTAL DESIGN FOR HYDRAZINE INHALATION EXPOSURE CONCENTRATIONS

Chamber hydrazine concentration (ppm)	Animal numbers, sex, and species
0.05	100 male, 100 female rats; 400 female mice
0.25	200 male hamsters; 400 female mice
0.25	100 male, 100 female rats; 4 male, 4 female dogs
1.0	200 male hamsters; 400 female mice
1.0	100 male, 100 female rats; 4 male, 4 female dogs
5.0	100 male, 100 female rats; 200 male hamsters
Control[a]	150 male, 150 female rats; 800 female mice; 200 male hamsters; 4 male, 4 female dogs

[a] Controls housed in a vivarium.

Rodents were maintained for as long a postexposure period as possible while sustaining sufficient numbers at final sacrifice for comparison of lesions in control and exposed groups. This resulted in postexposure holding times of 12 months for hamsters, 15 months for mice, and 18 months for rats. Dogs were held for a period of 38 months postexposure.

Test atmosphere introduction and analysis. Hydrazine was introduced into each chamber by means of an automatic syringe feeder. The syringe feeder metered the liquid hydrazine into a short ¼-in.-diameter Teflon tube connected to a ¼-in. stainless-steel tube leading to the chamber air introduction line. The Teflon and stainless-steel tubes were heated to 50°C using electrical heating tape. The slight chamber vacuum was sufficient to draw air through the introduction tube carrying the vaporized hydrazine into the air input to the chamber. The concentration in the atmosphere of each chamber was monitored using a Technicon Autoanalyzer proportioning pump and colorimeter as shown in Fig. 1. Chamber air was drawn through the absorbing tower, a 10-coil, ⅜-in. glass helix containing glass beads. A buffered iodine solution was pumped through the tower concurrently with chamber air. The solution contained 40 g/liter potassium iodide, 20 g/liter disodium phosphate, and 6 g/liter monopotassium phosphate. To this solution, 0.1 N iodine solution, made up in 40 g/liter potassium iodide, was added to give normalities ranging from 0.0001 to 0.001. Absorbances

[4] Jackson Laboratories, Bar Harbor, Maine.

[5] Charles River Breeding Laboratories, Wilmington, Mass.

[6] Engle Laboratory Animals, Inc., R.R. #2, Box 201-A, Farmersburg, Ind.

[7] Ridglan Farms, Inc., 301 West Main St., Mt. Horeb, Wisc.

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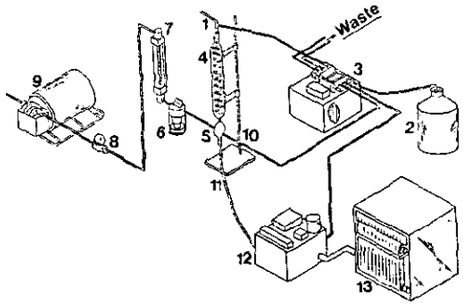

FIG. 1. Hydrazine analytical system. (1) sample line from chambers, (2) iodine absorber solution, (3) proportioning pump, (4) mixing coil, (5) phase separator, (6) filter, (7) flow meter, (8) control valve, (9) single-stage diapump, (10) waste line, (11) analysis sample line, (12) colorimeter, (13) strip chart recorder.

of the iodine solution were measured continuously at wavelengths of from 380 to 420 nm depending on the concentration. Hydrazine concentrations were determined after subtraction of the absorbances from baseline values measured by sampling chamber air for 2 hr before introduction of hydrazine. Over the year-long exposures, hydrazine concentrations were maintained with daily relative standard deviations of 10% or less in all chambers. Introduction of considerable excesses of hydrazine was required to attain the desired analytical concentrations. Mean nominal concentrations of 21, 5.5, 3.1, and 1.9 ppm were generated to attain time-weighted average analyzed concentrations of 4.96, 1.00, 0.25, and 0.05 ppm, respectively.

Parameters evaluated. All animals were observed hourly during the 12-month hydrazine exposure phase of the study and daily during the postexposure phase. Rats, dogs, and hamsters were weighed individually at biweekly intervals during exposure and monthly during the postexposure period. Mice were weighed in cage groups and group mean weights followed on a monthly schedule throughout the entire study.

Blood samples were drawn from the great saphenous veins of dogs at biweekly intervals during the exposure phase, and at 2, 5, 9, 14, 33, 83, 96, 121, and 152 weeks postexposure. Clinical determinations were made for the following battery of tests:

Red blood cell count	Total protein
White blood cell count	Albumin
Hematocrit	Globulin
Hemoglobin	A/G ratio
Sodium	Serum glutamic-pyruvic transaminase
Potassium	Alkaline phosphatase
Calcium	
Glucose	

Bromsulphalein (BSP) retention times were measured in all dogs at bimonthly intervals during the study.

All animals that died or were killed during the study were necropsied. The necropsy consisted of an external examination, including all body orifices, and the examination and fixation of portions of the tissues recommended by the National Cancer Institute (Sontag *et al.*, 1976). All tissues sampled were subjected to histopathologic examination. Tissues from each species of animal were examined by a single pathologist or by a group of pathologists who conferred and concurred on diagnoses. Histopathologic evaluation of nasal tissue was based upon a single, transverse section taken midway between the oral incisive papilla and the first palatal ridge.

Statistical analyses. Significance levels of differences between means of control and exposed groups for continuously variable parameters were determined using an independent *t*-test computer program (Dixon, 1983). For incidence data, significance levels of differences were computed using a Fisher's exact test program from the same source. Incidences of tumors compared were cumulative totals at final sacrifice. The patterns of mortality rate differences among groups were not such that this procedure would have led to underestimation of tumor incidence in exposed groups.

RESULTS

Clinical Determinations

Only hamsters experienced significant mortality during the exposure phase of the study. Each exposed group of hamsters had almost double the number of deaths during exposure as the control group (32–33% vs 19%). By study termination at 24 months from exposure start, however, mortality percentages among all groups were similar at 80–90%. In mice and rats, deaths during exposure were low in all groups (below 10%), and rat mortality at study end was similar in all groups (76–91%). Exposed mice demonstrated significantly higher mortality than controls at final sacrifice but without any relationship to dose (controls 72–79%; exposed 84–87%).

All groups of hamsters lost weight beginning at 12 months, with a maximum loss of 20 g at 15 months, i.e., 3 months after exposure termination. Thereafter, recovery to normal levels occurred by the 19th month. Since controls followed the same pattern, the weight loss apparently was not related to exposure. Diagnostic tests to identify specific causes for weight loss were inconclusive, but weights in all hamster groups at 24 months were not dif-

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ferent from those usually seen in animals of the same age. When compared with controls, weights of hamsters exposed to 5 ppm were severly depressed through the exposure and postexposure period until they attained parity with controls at 10 months postexposure. Hamsters exposed to 0.25 and 1.0 ppm hydrazine showed significant weight depression during exposure, but weights were not different from controls during the postexposure period. Exposed mice gained as much weight as controls during the exposure; however, all exposed groups gained less weight than controls during the postexposure period. Although the weights of male rats exposed to 5.0 ppm hydrazine were consistently lower than those of the other exposed groups, the major difference in weights was between controls and all the exposed groups. Female rats demonstrated no weight differences among groups until after exposure when controls outgained exposed groups by 20–30 g over the postexposure period.

Except for one dog, hematology and clinical chemistry differences between exposed and control dogs at any sampling period appeared random and not related to exposure. The exception, a male dog in the 1.0-ppm exposure group, exhibited intermittent increases in serum glutamic-pyruvic transaminase (SGPT) values beginning at 34 months postexposure. BSP retention time measured when these increases occurred was never greater than that of control animals nor was the liver palpable on examination. After multiple episodes of this cyclic event, the animal was sacrificed at 36 months postexposure and tissues examined. A control dog was also sacrificed for comparative pathology. Changes in the liver of the exposed dog were characterized as patchy to diffuse clusters of swollen hepatocytes that had highly vacuolated cytoplasm.

Nontumor Pathology

In male and female rats, the major nonneoplastic effects of exposure to hydrazine were mostly associated with the respiratory epithelium where inflammatory changes and squamous metaplasia were distinctly increased in the nose, larynx, and trachea of animals exposed at the 5.0-ppm level. No consistent increases in nontumor lesions occurred at exposures below 5 ppm, although squamous metaplasia was recorded with modest frequency in the nose of both control and exposed rats in all dose groups. Because controls were essentially free of changes characteristic of murine respiratory mycoplasmosis, this infectious disease was not believed to be a causative factor for respiratory changes documented in any group. In addition to respiratory lesions, increased inflammatory and degenerative changes were noted in the reproductive system of female rats exposed at the 5.0-ppm concentration. These and all other nonneoplastic lesions observed with significant frequency in rats are listed in Table 2.

The major nontumor pathologic change noted in hamsters was generalized amyloidosis which was manifest in the liver, kidneys, thyroid, and adrenal glands. This lesion was a common finding in control hamsters, but appeared with significantly greater frequency in exposed animals, usually showing positive dose dependence. Hemosiderosis and bile duct hyperplasia were also increased in the livers of exposed animals, as was senile atrophy in the testes. All these differences appeared to reflect an exposure-related acceleration of common aging changes in hamsters. Table 3 presents the incidence data for those hamster lesions showing significant increases in exposed animals.

In mice, no nonneoplastic effects of exposure were recorded, and the only nontumor lesion observed in dogs was in the previously described subject which exhibited focal areas of highly vacuolated liver cells and a corresponding elevation in SGPT values. It should be noted that these hepatocellular changes were considered to be highly compatible with steroid-induced hepatopathy in dogs (Fittschen and Bellamy, 1984).

Tumor Pathology

Neoplastic lesions in rats and hamsters which were observed with a significantly greater incidence in exposed subjects, or which

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TABLE 2

NONNEOPLASTIC LESIONS IN HYDRAZINE-EXPOSED MALE AND FEMALE RATS

Lesion	Incidence (%)				
	Control	0.05 ppm	0.25 ppm	1.0 ppm	5.0 ppm
Nasal					
Squamous metaplasia					
Males	24/146 (16)	19/96 (20)	24/94 (26)	25/97 (26)	47/99 (47)[a]
Females	28/145 (19)	18/97 (19)	23/98 (23)	24/94 (26)	28/95 (25)
Epithelial hyperplasia					
Males	4/146 (3)	9/96 (9)	3/94 (3)	4/97 (4)	21/99 (21)[a]
Females	3/145 (2)	2/97 (2)	4/98 (4)	5/94 (5)	9/95 (9)[b]
Larynx					
Squamous metaplasia					
Males	2/141 (1)	2/95 (2)	2/91 (2)	3/91 (3)	18/92 (20)[a]
Females	6/138 (4)	2/91 (2)	2/91 (2)	4/91 (4)	14/91 (15)[a]
Inflammation					
Males	14/141 (9)	42/95 (44)	7/91 (8)	14/91 (15)	72/92 (78)[a]
Females	22/138 (16)	11/91 (12)	4/91 (4)	10/91 (11)	48/91 (53)[a]
Trachea					
Squamous metaplasia					
Males	0/145 (0)	0/97 (0)	0/98 (0)	0/95 (0)	10/97 (10)[a]
Females	0/147 (0)	0/96 (0)	0/97 (0)	0/95 (0)	6/98 (6)[a]
Inflammation					
Males	5/145 (3)	17/97 (18)[a]	2/98 (2)	2/95 (2)	52/97 (54)[a]
Females	0/147 (0)	3/96 (3)	1/97 (1)	4/95 (4)[b]	29/98 (30)[a]
Lymph node					
Hyperplasia					
Males	4/149 (3)	5/99 (5)	3/99 (3)	5/98 (5)	5/99 (5)
Females	3/147 (2)	2/97 (2)	4/100 (4)	3/97 (3)	11/98 (11)[a]
Hepatic					
Focal cellular change					
Males	58/149 (39)	39/99 (39)	40/99 (40)	41/99 (41)	42/99 (42)
Females	57/147 (39)	42/97 (43)	36/100 (36)	58/97 (60)[a]	64/98 (65)[a]
Endometritis	8/147 (5)	5/97 (5)	0/100 (0)	6/97 (6)	21/98 (21)[a]
Salpingitis	0/147 (0)	0/97 (0)	0/100 (0)	1/97 (1)	20/98 (20)[a]
Ovarian atrophy	15/147 (10)	13/97 (13)	3/100 (3)	15/97 (15)	22/98 (22)[b]

[a] Incidence significantly greater than control, $p \leq 0.01$.
[b] Incidence significantly greater than control, $0.01 < p \leq 0.05$.

occurred in a dose-dependent manner, are recorded in Tables 4 and 5, respectively. For most tumors, the statistical significance of the increased frequency over controls was either nonexistent or borderline, as in the case of thyroid carcinoma in male rats (5.0-ppm level). In contrast, neoplasms of the nasal epithelium were distinctly increased in both rats and hamsters, with greater than 50% of the male rats exhibiting benign nasal tumors at the 5.0-ppm exposure concentration.

By far, the most frequently diagnosed nasal tumor in both rats and hamsters was the adenomatous polyp. In the rat, these benign neoplasms were often multiple and were approximately twice as common in males (59%)

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TABLE 3

NONNEOPLASTIC LESIONS IN HYDRAZINE-EXPOSED MALE HAMSTERS

Lesion	Incidence (%)			
	Control	0.25 ppm	1.0 ppm	5.0 ppm
Liver				
Amyloidosis	42/180 (23)	67/160 (42)[a]	68/148 (46)[a]	79/159 (50)[a]
Hemosiderosis	42/180 (23)	63/160 (39)[a]	77/148 (52)[a]	94/159 (59)[a]
Bile duct hyperplasia	14/180 (8)	31/160 (19)[a]	28/148 (19)[b]	44/159 (28)[a]
Biliary cyst	45/180 (25)	45/160 (28)	42/148 (28)	55/159 (35)[b]
Spleen				
Amyloidosis	39/160 (24)	39/129 (30)	57/130 (44)[a]	60/138 (44)[a]
Lymph nodes				
Lymphadenitis	6/167 (4)	13/143 (9)[b]	17/140 (12)[a]	16/146 (11)[a]
Kidney				
Interstitial amyloidosis	15/179 (8)	19/164 (12)	21/145 (15)	28/160 (18)[a]
Glomerular amyloidosis	39/179 (22)	53/164 (32)[b]	67/145 (46)[a]	77/160 (48)[a]
Mineralization	55/179 (31)	78/164 (48)[a]	51/145 (35)	82/160 (51)[a]
Thyroid				
Amyloidosis	9/155 (6)	20/117 (17)[a]	11/127 (9)	22/137 (16)[a]
Adrenal				
Amyloidosis	38/177 (22)	49/155 (32)[b]	52/141 (37)[a]	76/153 (50)[a]
Degeneration	25/177 (14)	29/155 (19)	26/141 (18)	34/153 (22)[b]
Testis				
Senile atrophy	33/185 (18)	41/160 (26)	40/149 (27)[b]	55/159 (35)[a]
Aspermatogenesis	27/185 (15)	20/160 (13)	18/149 (12)	36/159 (23)[b]
Hypospermatogenesis	33/185 (18)	35/160 (22)	38/149 (26)	41/159 (26)

[a] Incidence significantly greater than control, $p \leq 0.01$.
[b] Incidence significantly greater than control, $0.01 < p \leq 0.05$.

as in females (29%) exposed at the highest concentration. Sexual predisposition could not be established in hamsters because only males were exposed. In both species, these benign neoplasms usually presented as a broadly-based, noninvasive polypoid mass originating along the nasoturbinates and extending into the dorsal and/or ventral meatus with mild displacement of juxtaposed structures (Fig. 2). Microscopically, these tumors usually consisted of densely packed epithelial cells arranged in cordlike festoons or solid patterns, with proliferating cells often palisading about central, vascular channels. In many tumors, variably sized glandular acini were present which were often filled with cellular detritus, collections of degenerating neutrophils, and/or PAS-positive secretory material. Acini were usually lined by nonciliated, low columnar to cuboidal cells which blended into a surrounding matrix of undifferentiated epithelial cells (Fig. 3). Mitotic figures were relatively common. Supporting stroma was scanty to nonexistent and interstitial accumulations of both neutrophils and mononuclear inflammatory cells were frequent in some tumors. Additionally, some neoplasms exhibited focal areas of differentiation into both mucocytes and more squamoid cells, prompting a diagnosis of "mucoepidermoid" tumor to be considered (Figs. 4 and 5).

Although adenomatous polyps were the most common nasal tumors in both rats and hamsters, smaller but significant numbers of

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TABLE 4

TUMORS OCCURRING AT HIGHER INCIDENCES IN HYDRAZINE-EXPOSED RATS OVER CONTROLS

Tumor type	Control	0.05 ppm	0.25 ppm	1.0 ppm	5.0 ppm
Females					
Nasal adenomatous polyp	0/145	2/97	0/98	2/94	28/95[a]
Nasal villous polyp	0/145	0/97	0/98	2/94	2/95
Nasal adenocarcinoma	0/145	1/97	0/98	0/94	3/95
Nasal squamous cell papilloma	0/145	0/97	0/98	0/94	3/95
Nasal squamous cell carcinoma	0/145	0/97	0/98	0/94	2/95
Bronchial adenoma	0/145	0/97	0/98	0/94	1/95
Males					
Nasal adenomatous polyp	0/146	2/96	1/94	9/97[a]	58/98[a]
Nasal villous polyp	0/146	0/96	0/94	1/97	12/98[a]
Nasal adenocarcinoma	0/146	1/96	0/94	0/97	0/98
Nasal squamous cell papilloma	0/146	0/96	0/94	0/97	3/98
Nasal squamous cell carcinoma	0/146	0/96	0/94	1/97	2/98
Bronchial adenoma	0/146	0/96	0/94	0/97	3/98
Thyroid carcinoma	7/146	6/96	5/94	9/97	13/98[b]

[a] Incidence significantly greater than control, $p \leq 0.01$.
[b] Incidence significantly greater than control, $0.01 < p \leq 0.05$.

squamous cell tumors were also noted in the noses of rats exposed to 5.0 ppm hydrazine. Squamous neoplasms were not documented in the respiratory tracts of hamsters or mice although it is important to recognize that the highest exposure concentration for mice was 1.0 ppm. Additionally, three poorly differentiated adenocarcinomas and modest numbers

TABLE 5

TUMORS OCCURRING AT HIGHER INCIDENCE IN HYDRAZINE-EXPOSED HAMSTERS OVER CONTROLS

	Incidence (%)				
Tumor type	Control	0.05 ppm	0.25 ppm	1.0 ppm	5.0 ppm
Nasal					
Adenomatous polyp	1/181		0/154	1/148	16/160[a]
Thyroid					
Parafollicular cell adenoma	0/145		0/117	0/127	4/137
Colon					
Adenocarcinoma	0/158		0/146	2/129	3/139
Leiomyoma	0/158		0/146	0/129	1/139
Papilloma	0/158		0/146	0/129	1/139
Stomach					
Basal cell carcinoma	0/169		0/149	2/140	1/145

[a] Incidence significantly greater than control, $p \leq 0.01$.

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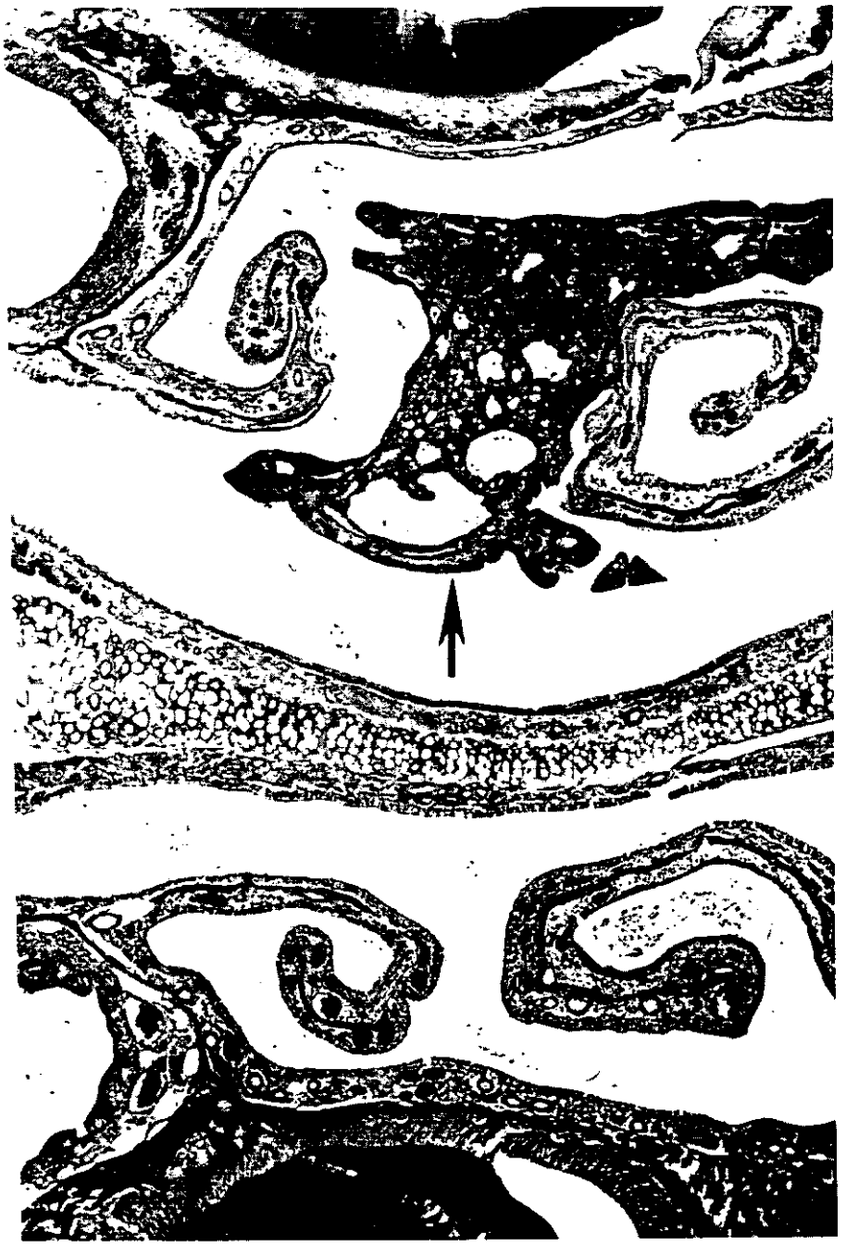

FIG. 2. Adenomatous polyp (arrow) in a male hamster originating along the nasoturbinates and extending into the dorsal/ventral meatus. H & E × 25.

of villous polyps were noted in exposed rats. Most rat nasal tumors, benign or malignant, were seen after 1 year of postexposure holding, with the earliest occurring in a male rat 20 months after exposure start and in a female 23 months following exposure start. In hamsters, neoplasms were also found in the thyroid and digestive system following hydrazine ex-

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FIG. 3. Typical male rat adenomatous polyp. Proliferating epithelial cells palasading along scanty fibrovascular stroma and forming acinar structures filled with secretory material and degenerating cells. H & E × 50.

posure (Table 5). Although the incidence values lack statistical significance, their occurrence only at the higher exposure levels is strong evidence of their resulting from hydrazine exposure. The only neoplastic lesions found in higher incidence in exposed mice were lung adenomas, and the increase was of borderline statistical significance at the 1.0-

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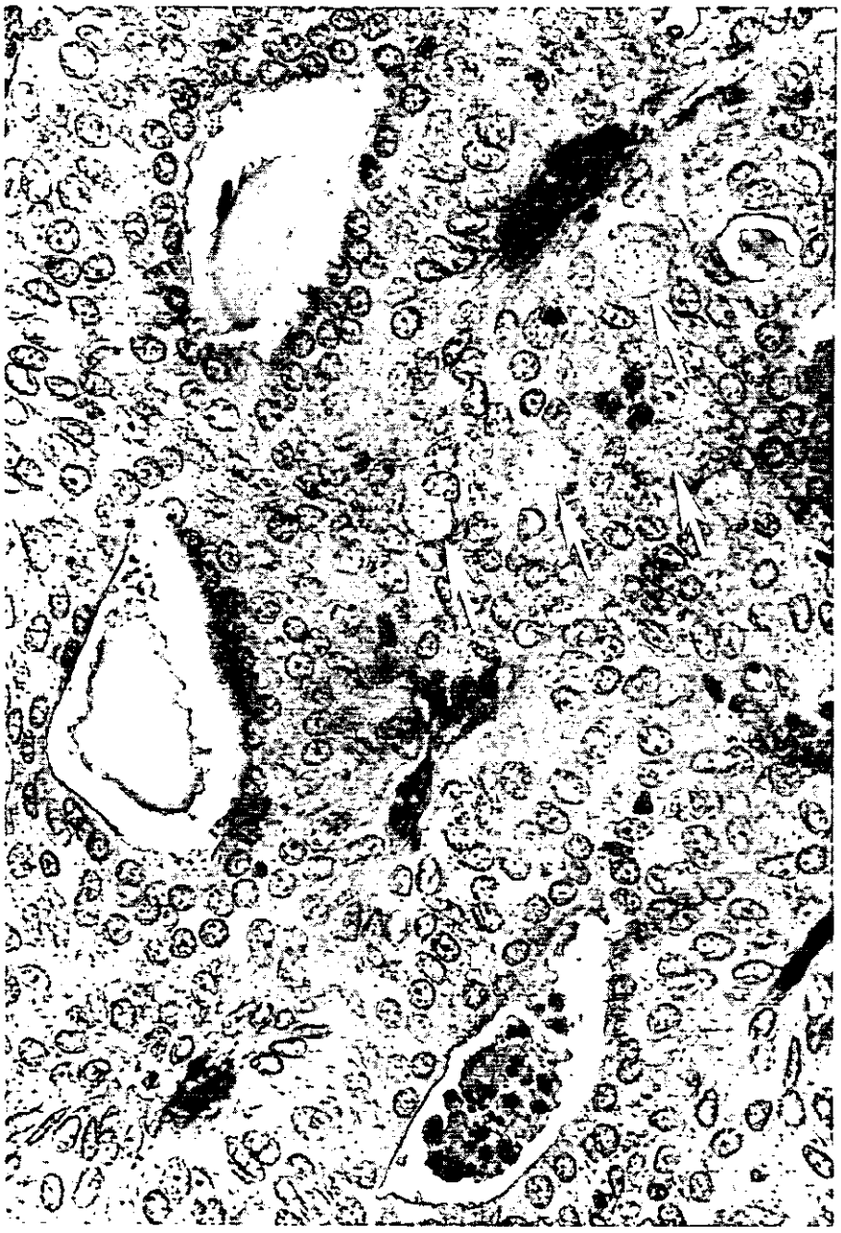

FIG. 4. Higher magnification of a male rat adenomatous polyp exhibiting early mucous cell differentiation (arrows). H & E × 100.

ppm level when concurrent controls were used for comparison (12/379 vs 4/378). This significance disappeared when the alternate group of controls (8/385) was used. A background incidence of 2–3% is common for pulmonary adenomas in all C57BL/6 mice used for experimental purposes in our laboratory. These observations, therefore, strongly suggest

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FIG. 5. Rat adenomatous polyp with early squamous cell differentiation. H & E × 100.

that the slight increase in lung tumors in mice at the highest level was probably a random event. As noted earlier, the mice were not exposed to 5.0 ppm because previous repeated exposures of mice to this level for 6 months caused 50% mortality.

Only two tumors were seen in dogs. Both were observed in one individual exposed to

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0.25 ppm hydrazine. One was diagnosed as an hemangioma of the splenic capsule, and the other was recorded as a papillary carcinoma of low-grade malignancy arising from the mucocutaneous border of the anus.

DISCUSSION

This study differed from those performed previously in one or more of the following factors: use of the inhalation route, the free base rather than the sulfate salt, and different strains of rats (Fischer 344) and mice (C57BL/6). Unexpectedly, mice were the most resistant species to the oncogenic effects of hydrazine, showing only a questionable increase in benign lung tumors at 1.0 ppm. This borderline increase of lung tumors in mice exposed to hydrazine contrasts with previous studies with hydrazine sulfate delivered per os in which mice developed significantly more lung tumors than other species at comparable levels of exposure. A previous report of hydrazine inhalation exposures (MacEwen *et al.*, 1974) indicated a dose-related increase in alveolargenic carcinomas in female mice exposed to 1.0 and 5.0 ppm hydrazine in a strain (ICR) that normally has a high incidence of these tumors.

Although the respiratory system appears to be the primary site of hydrazine-induced tumors in rats and mice, previous studies had shown the lung to be the specific target organ. Under our study conditions, the nasal cavities were the sites of the most striking tumor development. In rats, large numbers of dose-related benign tumors and, at the highest exposure level, modest numbers of malignant tumors of the nasal mucosa were characteristic of inhalation exposure to hydrazine. In hamsters, a species which was resistant to tumor development after oral administration of hydrazine sulfate in previous studies, a significant incidence of nasal polyps resulted from exposure to 5.0 ppm hydrazine. Small numbers of colon, stomach, and thyroid parafollicular cell tumors were also present in hamsters exposed to the higher concentrations of hydrazine, with none in controls or those exposed to 0.25 ppm. Rats exhibited a small increase in bronchial adenomas at the highest level of exposure, although statistical significance was not obtained because of the small numbers of tumors, one in females and three in males. These airway neoplasms had biological significance since no tumors appeared in controls or any subjects exposed to lower dose levels. No other tumor was induced or increased over natural incidence in any of the species tested.

The nasal polyps in rats and hamsters noted after 1 year high-level repeated exposures to hydrazine generally were not life threatening and represented only one among the many chronic toxic effects of the hydrazine exposure. The irritative effect of the higher level hydrazine concentrations is apparent from the greatly increased inflammatory response of the upper airways of both male and female rats. The inflammatory response was accompanied by an increase in squamous metaplasia of epithelial cells lining the trachea, larynx, and nasal passages. Similar effects have been noted with long-term exposure of Fischer 344 rats to formaldehyde (Kerns *et al.*, 1983). In that study, squamous cell carcinomas were induced in rats at an incidence of 43% after 24 months of intermittent exposure to 14.3 ppm formaldehyde. Both sexes were equally affected. Smaller numbers of benign polypoid adenomas also were detected in formaldehyde-exposed rats, but not in a distinctly dose-related fashion. These polypoid adenomas, however, did appear to have a striking morphologic similarity to the adenomatous polyps induced by exposure to hydrazine and, as with hydrazine, tumors were more prevalent in males than females. It should be noted that in hydrazine-exposed rats, benign nasal tumors outnumbered malignant neoplasms by 6 to 10 times. In formaldehyde-exposed subjects the trend was reversed.

In contrast to rats, we were unable to detect any exposure-related upper respiratory inflammation, hyperplasia, or metaplasia in dogs

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and mice, species that did not develop nasal tumors, or in hamsters, a species that did. Kerns *et al.* (1983) reported that mice exposed to 14.3 ppm formaldehyde for 2 years developed two squamous cell carcinomas in 45 animals examined. Epithelial dysplasia and metaplasia preceded and accompanied the development of tumors in formaldehyde-exposed mice. Chang *et al.* (1983) reported that the "dose" available for absorption in the nasal tissue of mice exposed to 15 ppm formaldehyde was reduced relative to that of rats by a significant depression of respiratory minute volume which did not occur in rats. Autoradiography of nasal tissues after exposure to [^{14}C]formaldehyde confirmed that less radioactivity per unit area was deposited in exposed mice than in exposed rats. In the present study, no measurements were made to determine whether similar decreases of hydrazine "dose" occurred in exposed mice. Rusch *et al.* (1983) exposed monkeys, rats, and hamsters to 0.2, 1.0, and 3.0 ppm formaldehyde for 26 weeks on a 22-hr/day, 7-day/week schedule. Rats and monkeys developed squamous metaplasia of the nasal turbinates, but hamsters showed no evidence of exposure-related effects.

There are similarities between the responses of rodents to formaldehyde (Chang *et al.*, 1983; Kerns *et al.*, 1983; Rusch *et al.*, 1983) and hydrazine as shown in our investigation. Rats are the most sensitive species to upper respiratory effects, neoplastic and nonneoplastic, of both compounds. Mice showed lower incidences of cellular change and neoplasia on 24-month exposure to 14.3 ppm formaldehyde than rats and no detectable pathological responses were present in the noses of mice after 12-month exposure to 1.0 ppm hydrazine. Hamsters exposed to 3 ppm formaldehyde almost continuously for 6 months reacted similarly to hamsters exposed to 5.0 ppm hydrazine intermittently for a year in that nontumor pathological responses were absent in the nasal respiratory epithelium. No tumors were detected in the hamsters exposed to formaldehyde, but this might be expected because the animals were exposed for a shorter period and not held past exposure termination. Like formaldehyde, hydrazine is a very water-soluble compound and, in the vapor state, might be expected to be absorbed by the first moist surface available to it when inhaled, the nasal mucosa. It is not surprising that the most sensitive target tissue for both compounds is the nasal epithelium.

We conclude from these long-term inhalation studies on male Golden Syrian hamsters, female C57BL/6 mice, and male and female Fischer 344 rats that hydrazine is capable of inducing nasal tumors, primarily benign, in rats and hamsters after 1-year intermittent exposure. Colon, stomach, and thyroid tumors in hamsters and bronchial adenomas in rats occurred in small numbers only at the highest levels tested.

REFERENCES

BIANCIFIORI, C. (1970a). Tumori polmonari ed epatici da idrazina solfato a dosi ridotte in topi BALB/c/Cb/Se. *Lav. Inst. Anat. Univ. Perugia* **30**, 89–99.

BIANCIFIORI, C. (1970b). Hepatomas in CBA/Cb/Se mice and liver lesions in Golden hamsters induced by hydrazine sulfate. *J. Natl. Cancer Inst.* **44**, 943–953.

BIANCIFIORI, C., BUCCIARELLI, E., CLAYSON, D. B., AND SANTILLI, F. E. (1964). Induction of hepatomas in CBA/Cb/Se mice by hydrazine sulphate and lack of effect of croton oil on tumor induction in BALB/c/Cb/Se mice. *Brit. J. Cancer* **18**, 543–550.

BIANCIFIORI, C., BUCCIARELLI, E., SANTILLI, F. E., AND RIBACCHI, R. (1963a). Carcinogenesi polmonare da irazide dell' acido isonicotinico (INI) e suoi metaboli in topi CBA/Cb/Se substrain. *Lav. Inst. Anat. Univ. Perugia* **23**, 209–220.

BIANCIFIORI, C., AND RIBACCHI, R. (1962). Pulmonary tumors in mice induced by oral isoniazid and its metabolites. *Nature (London)* **194**, 488–489.

BIANCIFIORI, C., RIBACCHI, R., BUCCIARELLI, E., DILEO, F. P., AND MILIA, U. (1963b). Cancerogenesi polmonare da idrazina solfato in tope femmine BALB/c. *Lav. Inst. Anat. Univ. Perugia* **23**, 115–128.

CHANG, J. C. F., GROSS, E. A., SIVENBERG, J. A., AND BARROW, C. S. (1983). Nasal cavity deposition, histopathology, and cell proliferation after single or repeated formaldehyde exposures in B6C3F1 mice and Fischer 344 rats. *Toxicol. Appl. Pharmacol.* **68**, 161–176.

CLARK, D. A., BAIRINGTON, J. D., BITTER, H. L., COE, F. L., MEDINA, M. A., MERRITT, J. H., AND SCOTT,

BNA08768176

HDMSP001793863

W. N. (1968). Pharmacology and toxicology of propellant hydrazines. In *Aeromedical Reviews,* Review 11–68. Aerospace Medical Division, Brooks Air Force Base, Tex.

DIXON, W. J. (1983). *BMDP Statistical Software, T-test-Program 3D, Fisher 10 exact test-Program 4F.* Univ. of California Press, Berkeley.

FITTSCHEN, C., AND BELLAMY, J. E. C. (1984). Prednisone-induced morphologic and chemical changes in the liver of dogs. *Vet. Pathol.* **21,** 399–406.

HAUN, C. C., AND KINKEAD, E. R. (1973). Chronic inhalation toxicity of hydrazine. In *Proceedings of the Fourth Annual Conference on Environmental Toxicology,* AMRL-TR-73-125, pp. 351–363. Wright–Patterson Air Force Base, Ohio.

HERBOLD, B. A., AND RÖHRBORN, G. (1977). Point mutation research: Relevance for humans. *J. Toxicol. Environ. Health* **2,** 1183–1191.

JONES, L. D., FAIRCHILD, D. G., AND MORSE, W. C. (1971). The induction of pulmonary neoplasms in mice by isonicotinic acid hydrazide. *Amer. Rev. Respir. Dis.* **103,** 612–617.

JUHASZ, J., BALO, J., AND SZENDE, B. (1963). Neue experimentelle Angaben zur Geschwulsterzeugenden Wirkung des Isonicotinsäurehydräzid (INH). *Z. Krebsforsch.* **65,** 434–438.

KELLY, M. G., O'GARA, R. W., YANCEY, S. T., GADEKAR, K., BOTKIN, C., AND OLIVIERO, V. T. (1969). Comparative carcinogenicity of *N*-isopropyl-α-(2-methylhydrazino)-*p*-toluamide HCl (procarbazine hydrochloride), its degradation products, other hydrazines and isonicotinic acid hydrazide. *J. Natl. Cancer Inst.* **42,** 337–344.

KERNS, W. D., DONOFRIO, D. J., AND PAVKOV, K. S. (1983). The chronic effects of formaldehyde inhalation in rats and mice: A preliminary report. In *Formaldehyde Toxicity.* (J. Gibson, ed.), pp. 111–131. Hemisphere, New York.

MACEWEN, J. D., MCCONNELL, E. E., AND BACK, K. C. (1974). The effects of 6-month chronic low level inhalation exposures to hydrazine on animals. In *Proceedings of the 5th Annual Conference on Environmental Toxicology,* AMRL-TR-74-125, pp. 225–235, Aerospace Medical Research Laboratory, Wright–Patterson Air Force Base, Ohio.

MORI, K., YASUNO, A., AND MATSUMOTO, K. (1960). Induction of pulmonary tumors in mice with isonicotinic acid hyrazide. *Gann* **51,** 83–90.

PATRICK, R. L., AND BACK, K. C. (1965). Pathology and toxicology of repeated doses of hydrazine and 1,1-dimethylhydrazine in monkeys and rats. *Ind. Med. Sarg.* **34,** 430–435.

PEACOCK, A., AND PEACOCK, P. R. (1966). The results of prolonged administration of isoniazid to mice, rats and hamsters. *Brit. J. Cancer* **20,** 307–325.

ROE, F. J. C., GRANT, A. G., AND MILLICAN, D. M. (1967). Carcinogenicity of hydrazine and 1,1-dimethylhydrazine for mouse lung. *Nature (London)* **216,** 375.

ROGERS, A. M., AND BACK, K. C. (1981). Comparative mutagenicity of hydrazine and three methylated derivatives in L517BY mouse lymphoma cells. *Mutat. Res.* **89,** 321–328.

RUSCH, G. M., CLARY, J. J., RINEHART, W. F., AND BOLTE, H. F. (1983). A 26-week inhalation toxicity study with formaldehyde in the monkey, rat, and hamster. *Toxicol. Appl. Pharmacol.* **68,** 329–343.

SEVERI, L., AND BIANCIFIORI, C. (1968). Hepatic carcinogenesis in CBA/Cb/Se mice and Cb/Se rats by isonicotinic acid hydrazide and hydrazine sulfate. *J. Natl. Cancer Inst.* **41,** 331–349.

SONTAG, J. M., PAGE, N. B., AND SAFFIOTTI, U. (1976). *Guidelines for Carcinogen Bioassay in Small Rodents,* NCI-CG-TR-1, pp. 52–55. U.S. Department of Health, Education, and Welfare.

THOMAS, A. A. (1965). Low ambient pressure environments and toxicity. *AMA Arch. Environ. Health* **11,** 316–322.

TOTH, B. (1969). Lung tumor induction and inhibition of breast adenocarcinomas by hydrazine sulfate in mice. *J. Natl. Cancer Inst.* **42,** 469–475.

TOTH, B. (1971). Investigations on the relationship between chemical structure and carcinogenic activity of substituted hydrazines. *Proc. Amer. Assoc. Cancer Res.* **12,** 55.

TOTH, B. (1972). Tumorigenesis studies with 1,2-dimethylhydrazine dichloride, hydrazine sulphate and isonicotinic acid in Golden hamsters. *Cancer Res.* **32,** 804–807.

TOTH, B., AND SHUBIK, P. (1966). Carcinogenesis in Swiss mice by isonicotinic acid hydrazide. *Cancer Res.* **26,** 1473–1475.

TOTH, B., AND SHUBIK, P. (1969). Lack of carcinogenic effects of isonicotinic acid hydrazide in the Syrian Golden hamster. *Tumori* **55,** 127–136.

TOTH, B., AND TOTH, T. (1970). Investigation on the tumor producing effect of isonicotinic acid hydrazide in ASW/Sn mice and MRC rats. *Tumori* **56,** 315–325.

WADE, D. R., LOHMAN, P. H. M., MATTERN, I. E., AND BERENDS, F. (1981). The mutagenicity of isoniazid in Salmonella and its effects on DNA repair and synthesis in human fibroblasts. *Mutat. Res.* **89,** 9–20.

WALD, N., BOREHAM, J., DOLL, R., AND BONSALL, J. (1984). Occupational exposure to hydrazine and subsequent risk of cancer. *Brit. J. Med.* **41,** 31–34.

WITKIN, L. B. (1956). Acute toxicity of hydrazine and some of its methylated derivatives. *Arch. Ind. Health* **13,** 34.

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Occupational exposure to hydrazine and subsequent risk of cancer

Joan Morris, James W Densem, Nicholas J Wald, Richard Doll

Abstract

***Objectives*—The aim was to examine the cause specific mortality of men exposed to hydrazine.**

***Methods*—Hydrazine was produced at a factory in the east midlands between 1945 and 1971. The cohort of all 427 men who were employed there for at least six months with varying degrees of occupational exposure to hydrazine were followed up until the end of January 1992.**

***Results*—By the end of July 1982 49 deaths had occurred and the observed mortality was found to be close to that expected at each level of exposure. By the end of January 1992 a further 37 deaths had occurred. Again the observed mortality was close to that expected for all causes and also for lung cancer, cancers of the digestive system, other cancers, and all other causes, irrespective of the level of exposure.**

***Conclusions*—The results weigh against there having been any material hazard of occupational exposure to hydrazine. The small number of men studied means, however, that a relative risk as high as 3·5 for lung cancer cannot confidently be excluded.**

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Keywords: occupational exposure; hydrazine; cancer

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Hydrazine (N_2H_4) is a colourless, fuming, oily liquid with an ammonia like odour. It is used as a polymerisation catalyst, a blowing agent, a reducing agent, and an oxygen scavenger in treatment of boiler water; in the synthesis of maleic hydrazide; and in the manufacture of drugs. Hydrazine is also used as a rocket propellant. The hydrazine bases are used in the production of salts and hydrazones that are used in surfactants, detergents, plastisers, pharmaceuticals, insecticides, and herbicides.

Both the International Agency for Research on Cancer[1] and the National Institute of Environmental Health Sciences[2] find that there is sufficient evidence for the carcinogenicity of hydrazine in experimental animals, but inadequate evidence for its carcinogenicity in humans. Oral hydrazine tested in mice and rats produced liver, mammary, and lung tumours in mice and lung and liver tumours in rats.[3,4] When tested by inhalation in concentrations comparable with occupationally exposed men (0·25–5ppm), it produced benign and malignant nasal tumours in rats, benign nasal polyps, a few colon tumours and thyroid adenomas in hamsters, and a slight increase in the incidence of lung adenomas in mice.[5]

The only observations available to test the carcinogenicity of hydrazine to humans have been those on 427 men who worked at a hydrazine plant in the east midlands region of the United Kingdom, who were followed up for an average of 20 years.[6] Mortality from all causes was not increased over that expected, but two lung cancers were found compared with 1·51 expected in men in the highest exposure category. The study had very little power to detect even a large hazard, because the number of deaths observed was so small. It has therefore been extended by following up the men for a further 10 years.

Details of hydrazine production at the factory between 1945 and 1971 have been given previously.[6] No measurements of atmospheric hydrazine were ever carried out, but the concentration of hydrazine is thought likely to have been 1–10 ppm in the general plant area and much higher than this ($\leqslant$100 ppm) close to the hydrazine storage vessels.

Method

Factory records showed that 427 men were employed there for at least six months during the period of hydrazine production. For each of these men, the following information was sought: identifying details, date of birth, date of first employment, date of leaving the company, and an estimate of the extent of hydrazine exposure based on the knowledge of the factory works manager. Each type of employment was classified in one of the following categories, according to the estimated degree of exposure.

HIGH EXPOSURE

Exposure was associated with the direct manufacture of hydrazine or of its derivatives, or involved the use of liquid hydrazine as a raw material. Exposure to hydrazine vapour was potentially the greatest for men in this category, who may have been exposed to about 1–10 ppm in the ambient air.

MODERATE EXPOSURE

Exposure was associated with an incidental presence in an area of the plant concerned with the manufacture of hydrazine or its derivatives (fitters and engineers, for example). Exposure in this category was unlikely to

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have been more than 1 ppm and was probably < 0·5 or 1 ppm for most of their employment.

LOW EXPOSURE

Little or no exposure occurred as men in this category were unlikely to have been exposed to hydrazine more than slightly, and then only infrequently.

Table 1 Numbers of men exposed and man-years at risk by category of exposure, duration of exposure, and years since first exposure

Category	Durations of Exposure*	Years since first exposure	Men (n)	Man-years (n)
High‡	⩾2 y	<10	54	508
		⩾10	50	878
	<2 y	<10	78	350
		⩾10	73	409
	All	<10	78	858
		⩾10	73	1287
Moderate and low‡	All	<10	375	3365
		⩾10	342	6154
All	All	<10	427†	4222
		⩾10	389	7441

*All men were exposed for ⩾6 months.
†Men who at first had low or moderate exposures and who were subsequently highly exposed contributed man-years at risk in the low or moderate categories initially and to the high category after their first exposure in that category. The numbers of men in each category, therefore, add up to more than 427 in all, as some men contributed to more than one category. Similarly, all men who contributed man-years at risk ⩾10 y after first exposure and for durations of exposure of ⩾2 y also contributed to man-years at risk <10 y after first exposure and to <2 y duration of exposure.
‡High = men who may have been exposed to about 1–10 ppm hydrazine vapour in the ambient air; moderate = men unlikely to have been exposed to ⩾1 ppm and probably <0·5 ppm hydrazine vapour in the ambient air; low = men unlikely to have been exposed to hydrazine vapour.

Table 2 Numbers of deaths observed (O) and expected (E) by category of exposure, duration of exposure, years since first exposure, and cause

Cause of death	Category of exposure	Duration of exposure	Years since first exposure	Deaths O (n)	Deaths E (n)	O/E
Lung cancer	High	⩾2 y	⩾10	1	2·11	0·47
			All	1	2·42	0·41
		All	⩾10	3	2·43	1·23
			All	3	2·79	1·08
	Moderate or low	All	⩾10	5	8·32	0·60
			All	5	9·27	0·54
	All	All	⩾10	8	10·76	0·74
			All	8	12·06	0·66
Cancer of digestive system	High	⩾2 y	⩾10	0	1·64	0·0
			All	0	1·86	0·0
		All	⩾10	0	1·90	0·0
			All	0	2·16	0·0
	Moderate or low	All	⩾10	8	6·54	1·22
			All	9	7·29	1·24
	All	All	⩾10	8	8·44	0·95
			All	9	9·45	0·95
Other cancer	High	⩾2 y	⩾10	2	1·82	1·10
			All	2	2·01	0·99
		All	⩾10	2	2·13	0·94
			All	2	2·40	0·83
	Moderate or low	All	⩾10	5	7·27	0·69
			All	6	8·14	0·74
	All	All	⩾10	7	9·39	0·75
			All	8	10·54	0·76
IHD	High	⩾2 y	⩾10	7	6·60	1·06
			All	8	7·39	1·08
		All	⩾10	7	7·60	0·92
			All	8	8·54	0·94
	Moderate or low	All	⩾10	16	25·82	0·62
			All	18	28·46	0·63
	All	All	⩾10	23	33·42	0·69
			All	26	37·00	0·70
Other causes	High	⩾2 y	⩾10	7	8·34	0·84
			All	7	9·53	0·73
		All	⩾10	7	9·35	0·75
			All	7	10·99	0·64
	Moderate or low	All	⩾10	24	28·54	0·84
			All	28	34·07	0·82
	All	All	⩾10	21	37·89	0·55
			All	35	45·06	0·78
All causes	High	⩾2 y	⩾10	17	20·51	0·83
			All	18	23·21	0·78
		All	⩾10	19	23·41	0·81
			All	20	26·88	0·74
	Moderate or low	All	⩾10	58	76·49	0·76
			All	66	87·23	0·76
	All	All	⩾10	77	99·90	0·77
			All	86	114·11	0·75

The men were followed up to the end of January 1992 through the cooperation of the Office of Population Censuses and Surveys by flagging their National Health Service records in the National Health Service Central Register at Southport.

It was possible to trace 406 (95%) of the 427 men. The 21 untraced men were excluded from the study from the last date they were known to have been living at the last known address, or, in the case of four men for whom this date was missing, from the last date of their employment in the factory. These dates were all before July 1982 (the cut off date for the previous analysis). Men who were first exposed in the low or moderate categories and who were subsequently exposed in the high category contributed man-years at risk in the low or moderate categories initially and to the high category after their first exposure in that category. Similarly, all men who contributed man-years at risk >10 years after first exposure and for durations of exposure of two years or more also contributed to man-years at risk <10 years after first exposure and to less than two years' duration of exposure.

Person-years at risk and death rates were calculated by five-year age groups and time since first exposure (<10 and ⩾10 years). The expected number of deaths was calculated from the death rates of men in England and Wales in the same five-year age bands over the same period of time. The overall death rates in the area in which the factory was located were similar to those in England and Wales. The observed and expected numbers of deaths were compared and tested for significance with one sided Poisson tests. The results for the period < 10 years since first exposure have been reported previously and are not reported here.

The death rates in those men who had the greatest exposure (high exposure for more than two years) were also compared to the death rates for all other men with Kaplan-Meier product limit analysis. Cox's proportional hazards regression analysis was not carried out due to the lack of fit of the models.

Results

Table 1 shows the number of man-years under observation according to the category of exposure, duration of exposure, and the number of years since first exposure. Of the 11664 man-years 18% at risk were in the high exposure category.

Table 2 shows the numbers of deaths observed compared with the numbers expected. The observed mortality is close to that expected for lung cancer, cancers of the digestive system, other cancers, and all other causes. For men in the highest exposure category the upper 95% confidence intervals (95% CIs) for the relative risks were: 3·61 for lung cancer, 1·94 for cancers of the digestive system, 1·90 for ischaemic heart disease, and 1·27 for mortality from all causes.

Log rank test statistics from non-parametric survival analysis showed that men with

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Table 3 Mantel-Haenszel [illegible] of observed and expected numbers of deaths from [illegible] for men exposed to hydrazine for >2 y compared with all other men

Cause of death	χ^2	P value
Lung cancer	0·04	0·85
Cancers of the digestive system	1·36	0·24
All cancer	0·10	0·75
All causes	3·21	0·07

the highest exposure did not seem to have significantly different mortalities for lung cancer, cancers of the digestive system, and all causes, compared with all the other men in the study (table 3).

Discussion

The only categories in which the number of observed deaths exceeded expected deaths (but not significantly) are lung cancer in men in the high exposure category for six months or more (three observed *v* 2·43 expected) and cancers of the digestive system in men in the low or moderate exposure category (eight observed *v* 6·54 expected). Two of the three deaths from lung cancer in men in the high exposure category were in men exposed in that category for less than two years. Only one case, however, occurred in men exposed in the high exposure category for more than two years *v* 2·11 expected. No cancers of the digestive system occurred in men with exposure in the high exposure category. No deaths occurred from nasal cancer.

A similar study in France of 140 men working at a plant producing hydrazine since 1962 reached similar conclusions (personal communication; Cordier S, Grand C, Contassot J-C). No significant excess in incidence of cancer was observed in the cohort of workers in comparison with the numbers expected from local cancer incidences. As in our study, however, an excess of digestive cancers was found in the low exposure group (three cases observed *v* 0·52 expected; P = 0·02). A significant excess of head and neck cancers (ICD-8 140-9) in the high exposure category was also found in the French study (two cases observed *v* 0·27 expected; P = 0·03), but no death from these causes was found in our study (0·49 expected). No excess of respiratory cancers was observed in the French study (we found one case *v* 1·29 expected).

Conclusions

The numbers of men exposed to hydrazine in both this and the French study were small. The results obtained are encouraging in that no obvious hazard from lung cancer or any other disease has appeared up to 46 years later. The study can confidently exclude a relative risk of lung cancer of about 3·5 or more, but the power of the study is too limited to exclude lower relative risks.

We thank Dr J Bonsall, former medical officer at FBC Limited, Hauxton, Cambridge, UK, for all his work on the study. We also thank National Aeronautics and Space Administration, Houston, Texas, for financial support for this project.

1 *IARC Monogr Eval Carcinog Risks Hum Suppl* 1988; 7:223–4.
2 National Institute of Environmental Health Sciences. *Fifth annual report on carcinogens [summary].* Research Triangle Park, NC: DHHS Public Health Service, 1989. (NTP 89;239:166–8)
3 *IARC Monogr Eval Carcinog Risks Hum* 1976;4:127–36.
4 Menon MM, Bhide SV. Perinatal carcinogenicity of izoniazid (INH) in Swiss mice. *J Cancer Res Clin Oncol* 1983;5:1050–64.
5 Vernot EH, MacEwan JD, Bruner RH, Haun CC, Kinkead ER, Prentice DE, *et al.* Long-term inhalation toxicity of hydrazine. *Fundam Appl Toxicol* 1985;5: 258–61.
6 Wald N, Boreham J, Doll R, Bonsall J. Occupational exposure to hydrazine and subsequent risk of cancer. *Br J Ind Med* 1984;41:31–4.

Vancouver style

All manuscripts submitted to *Occup Environ Med* should conform to the uniform requirements for manuscripts submitted to biomedical journals (known as the Vancouver style.)

Occup Environ Med, together with many other international biomedical journals, has agreed to accept articles prepared in accordance with the Vancouver style. The style (described in full in the *BMJ*, 24 February 1979, p 532) is intended to standardise requirements for authors.

References should be numbered consecutively in the order in which they are first mentioned in the text by Arabic numerals above the line on each occasion the reference is cited (Manson[1] confirmed other reports[2-5] . . .). In future references to papers submitted to *Occup Environ Med* should include: the names of all authors if there are seven or less or, if there are more, the first six followed by *et al*; the title of journal articles or book chapters; the titles of journals abbreviated according to the style of *Index Medicus*; and the first and final page numbers of the article or chapter. Titles not in *Index Medicus* should be given in full.

Examples of common forms of references are:

1 International Steering Committee of Medical Editors, Uniform requirements for manuscripts submitted to biomedical journals. *Br Med J* 1979;1:532–5.
2 Soter NA, Wasserman SI, Austen KF. Cold urticaria: release into the circulation of histamine and eosinophil chemotactic factor of anaphylaxis during cold challenge. *N Engl J Med* 1976;294:687–90.
3 Weinstein L, Swartz MN. Pathogenic properties of invading micro-organisms. In: Sodeman WA Jr, Sodeman WA, eds. *Pathologic physiology, mechanisms of disease.* Philadelphia: W B Saunders, 1974:457–72.

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Ann. occup. Hyg. Vol. 21, pp. 323–326.
Pergamon Press Ltd. 1978. Printed in Great Britain

LETTER TO THE EDITOR

HYDRAZINE

Sir,

In mice, exposure to hydrazine sulphate by mouth or intraperitoneal (i.p.) injection increased the incidence of three kinds of neoplasm to which mice are particularly subject, namely, lung tumours, liver tumours and malignant lymphoma (KELLY *et al.*, 1969; JUHASZ *et al.*, 1967; BIANCIFIORI, 1971; YAMAMOTO and WEISBURGER, 1970; BIANCIFIORI, 1970a; BIANCIFIORI and RIBACCHI, 1962; BIANCIFIORI, 1970b; BIANCIFIORI, 1970c; BIANCIFIORI *et al.*, 1964). Two experiments in hamsters yielded negative results in respect of tumorigenicity (BIANCIFIORI, 1970c; TOTH, 1972). Two out of 17 rats exposed to hydrazine sulphate by i.p. injection developed lung tumours which rarely arise spontaneously in this species (RIBACCHI and GIRALDO, 1968). In another experiment in rats, in which hydrazine sulphate was administered by lavage, both lung and liver tumours were seen (SEVERI and BIANCIFIORI, 1968). No long term experiment involving the exposure of laboratory animals to hydrazine vapour by the inhalation route has yet been reported, although studies of this kind in four different species are currently in progress and the results are expected during the next 12 months.

In 1974 representatives of nine manufacturers of hydrazine (I–IX) from five countries began to meet informally to exchange information concerning the health of workers who had been, or were currently being, exposed to hydrazine. Four of the nine companies started manufacturing hydrazine during or after 1960 and thus had no data relevant to the assessment of possible cancer risk. Five companies (III, VI, VII, VIII and IX) started manufacturing hydrazine on dates ranging from 1940 to 1956. These are discussed below.

Company III had records of all of the 53 men engaged in hydrazine manufacture for more than 10 yr between 1940 and 1974. Of the 35 men (mean age = 50 in 1974, average exposure = 15 yr, and average interval since first exposure = 21 yr) whose exposure began before 1963, two died before January 1975. Both deaths (at ages 48 and 60) were from heart disease. Anecdotal information from three other companies provided no grounds for suspecting any increased cancer risk. However, no basis has so far been made available to me for calculating expected numbers of deaths from cancer in any of these four companies.

Only one of the companies (Company VI) has, so far, initiated a more systematic epidemiological survey of its workers. This company operated a hydrazine manufacturing plant between 1945 and 1970 and had records of all of the 423 men who had worked at the plant during that period. Of the 423, 64 had been employed directly in the manufacture of hydrazine or on other plants in the same building and were regarded as 'most exposed'. A second, intermediately exposed, group of 189 consisted of men either employed for only a proportion of their time in the hydrazine

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TABLE 1. PRELIMINARY DATA FROM COMPANY VI

Extent of exposure to hydrazine	Length of exposure (yr)	Number of men	Men traced up to 30 June 1973						Untraced men		
			Number of men	Mean age (yr)	Number over 50 yr old on 30.6.73	Expected number of deaths*	Observed number of deaths	Deaths from cancer	Number of men	Mean age on 30.6.73	Number over 50 yr old on 30.6.73
Most	10+	10	10 (100%)	59.6	8	1.8	0	0	0	—	—
	<10	54	33 (61%)	45.8	14	2.6	4	0	21	42.6	5
Intermediate	10+	47	43 (91.5%)	54.1	28	9	6 } 10	0	4	52.5	3
	<10	142	84 (59%)	42.6	25		4	1†	58	36.5	6
Least	10+	28	26 (93%)	47.3	12	4.5	1 } 4	0	2	52.5	1
	<10	142	76 (53.5%)	38.5	20		3	1‡	66	40.1	10
		423	272 (64%)		107	17.9	18	2	151		25

* For method of calculation, see text. N.B. Separate figures for subgroups of intermediate and least exposed groups not available.
† Cancer of stomach at age 59.
‡ Neurogenic at age 22.

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manufacturing area (e.g. fitters) or in other buildings where hydrazine was handled, mainly in liquid form, in the course of the manufacture of hydrazine derivatives. The remaining 170 men were not involved either in the manufacture or use of hydrazine. Their exposure to hydrazine was limited to the fact that they were employed at the same factory. They were categorized as 'least exposed'. The three groups were subdivided according to whether men had qualified as members of the groups for more or less than 10 yr prior to 1970. By indirect methods (checking electoral registers, searching for death certificates, etc.) 272 (64%) of the 423 men were ascertained to be alive or dead on 30 June 1973. Of those traced 18 had died, and two of these from cancers (one in the intermediate exposure group and one in the least exposed group). The age of each man at the time he began to work in the factory was known. By the use of English Life Table No. 12, 1960162 in the Annual Abstract of Statistics, 1973, which shows, for each quinquennial age-cohort, proportions of men expected to survive until various ages, and by linear interpolation from these tables, expected numbers of deaths among the men of each category who were actually traced (i.e. found either alive or dead) could be calculated (see Table 1). The observed and expected numbers of deaths were similar. Since 30 June 1973, eight of the 254 men known to be alive on 30 June 1973 are known to have died. Three of the deaths were from malignant disease (Intermediate Group 10+ with cancer of stomach at age 74; Intermediate Group <10 with cancer of the stomach at age 64; Least exposed Group 10+ with cancer of the prostate at age 58). A systematic follow-up of the remaining 246 men is in progress and an attempt is being made to trace the 151 men shown as untraced in Table 1.

While the existing data are crude and incomplete, I consider that they at least provide evidence that these past occupational exposures to hydrazine were not associated with any greatly increased risk of cancer. Attempts are currently being made to extract further data from the records of all the companies concerned, to keep under surveillance all present hydrazine workers and all past hydrazine workers who have already been traced and to monitor the health of all men currently employed in hydrazine manufacture. Certain fundamental deficiencies in data from the past can never be made good; in particular, it will not be possible to measure retrospectively the extent of exposure of men to hydrazine. Anecdotal evidence, however, indicates that concentrations of hydrazine vapour in ambient air in factories have in the past been many times higher than the 0.1 ppm maximum level which all nine companies currently claim to be achieving. The purpose of this letter is to describe what has been done so far and to indicate that research is in progress.

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REFERENCES

BIANCIFIORI, C. (1970a) *Lav. Inst. Anat. Istol. Patol. Univ. Perugia* **30**, 137–146.
BIANCIFIORI, C. (1970b) *J. nat. Cancer Inst.* **45**, 965–970.
BIANCIFIORI, C. (1970c) *J. nat. Cancer Inst.* **44**, 943–949.
BIANCIFIORI, C. (1971) *Lav. Inst. Anat. Istol. Patol. Univ. Perugia* **31**, 79–90.
BIANCIFIORI, C., BUCCIARELLI, E., CLAYSON, D. B. and SANTILLI, F. E. (1964) *Br. J. Cancer* **18**, 543–550.
BIANCIFIORI, C. and RIBACCHI, R. (1962) *Nature* **194**, 488–489.

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HDMSP001793870

JUHASZ, J., BALO, J. and SZENDE, B. (1967) *Magy Onkol.* **11**, 31–36.
KELLY, M. G., O'GARA, R. W., YANCEY, S. T., GADEKAR, K., BOTKIN, C. and OLIVERIO, V. T. (1969 *J. nat. Cancer Inst.* **42**, 337–344.
RIBACCHI, R. and GIRALDO, G. (1968) *Lav. Ist. Anat. Istol. Patol. Univ. Perugia* **21**, 5–19.
SEVERI, L. and BIANCIFIORI, C. (1968) *J. nat. Cancer Inst.* **41**, 331–340.
TOTH, B. (1972) *Cancer Res.* **32**, 804–807.
YAMAMOTO, R. S. and WEISBURGER, J. H. (1970) *Life Sci.* **9**, Part II, 285–289.

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British Journal of Industrial Medicine 1984;**41**:31–34

Occupational exposure to hydrazine and subsequent risk of cancer

N WALD,[1] JILLIAN BOREHAM,[1] R DOLL,[1] AND J BONSALL[2]

From the ICRF Cancer Epidemiology and Clinical Trials Unit,[1] University of Oxford, Radcliffe Infirmary, Oxford, and Occupational Health Department,[2] FBC Limited, Hauxton, Cambridge, UK

ABSTRACT Four hundred and twenty seven men with varying degrees of occupational exposure to hydrazine, a weak animal carcinogen, were studied to see if they provided any evidence of carcinogenicity to man. The observed mortality was close to that expected for lung cancer, other cancers, and all other causes, irrespective of the level of exposure. There were 49 deaths (61·47 expected) from all causes including five deaths from lung cancer (6·65 expected). The results show that no obvious hazards associated with hydrazine exposure have yet appeared but because of the small number of men studied they can only exclude gross hazards.

Hydrazine (N_2H_4) is a colourless, fuming, oily liquid with an ammonia like odour. The estimated total world production in 1981 was 30 000 tons. About 75% of hydrazine is used as a chemical intermediate in the production of pesticides or plastic additives, about 10% is used in fine chemical manufacture (particularly in the production of isoniazid and allopurinol), and the remaining proportion is used as a deoxygenating material for boiler-feed water and as a propellant in rocketry.

Hydrazine has been categorised by the International Agency for Research on Cancer as a weak carcinogen[1] and by the American Conference of Governmental Industrial Hygienists (ACGIH) as an industrial substance suspected of carcinogenic potential for man.[2 3] The evidence is based largely on the administration of hydrazine and its sulphate salts to rodents.

Mice given hydrazine sulphate by mouth at up to 45 mg/kg/day showed a dose related increase in the incidence of hepatoma, mostly "hepatocarcinomas."[4 5] Hydrazine, at doses around 25 mg/kg/day, has also been shown to cause myeloid leukaemia, reticulum cell sarcoma of the mediastinum, and pulmonary adenomas and lymphomas.[6–8] Rats fed 3–4·4 mg/day over a 68 week period showed an increased incidence of lung adenomas and carcinomas, and an increased incidence of liver tumours.[4 9]

Oral administration of hydrazine sulphate to hamsters, however, did not cause a significant excess of cancers, but 1,2-dimethyl hydrazine did cause angiosarcomas of blood vessels and caecal and hepatic tumours.[5 10]

Rats exposed for one year to hydrazine vapour by inhalation in concentrations comparable to occupationally exposed men (0·25–5 ppm), and then kept for their normal lifespan, showed an increased incidence of benign and macroscopically malignant tumours in the nose, the incidence of which was dose dependent. Mice and hamsters similarly exposed showed an increased incidence of lung adenomas and of nasal polyps respectively.[11]

It seemed highly desirable, therefore, to see whether there was any evidence that hydrazine was carcinogenic to man and to see what had happened to men who had been exposed to hydrazine vapour in the course of their work, even if the number available for study was small. A preliminary analysis of men working at a hydrazine plant failed to suggest an excess risk of cancer associated with exposure to hydrazine.[12] The follow up was incomplete, however, and as mortality was not analysed by cause we conducted a fresh study using the same cohort.

The plant

At a factory in the east Midlands between 1945 and 1971 about 700 tons of hydrazine were produced a year. The plant was in an enclosed building and, as hydrazine was not considered to be more hazardous than ammonia, exhaust ventilation was not provided. Hydrazine was kept in open tanks and hydrazine compounds were made from strong hydrazine solutions in open vessels, which were heated to

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enhance evaporation. Packing of hydrazine into small commercial containers was carried out in the same building. Spillages were not necessarily flushed away immediately, and it was the practice of the laboratory workers to pipette hydrazine solutions by mouth.

Unfortunately, no measurements of atmospheric hydrazine were ever carried out at this plant, although the level of hydrazine is likely to have been from 1 to 10 ppm in the general plant area and levels much higher than this (up to 100 ppm) may have occurred close to hydrazine storage vessels. These estimations have been derived by the simulation of spillages and calculations using data on the saturated vapour pressure of hydrazine at 20°C, which suggest that maximum levels of 100 ppm are possible. Other organic chemicals were also manufactured in the same factory.

Method

Factory records showed that 427 men were employed there for at least six months during this period. For each of these men the following information was sought: identifying details, date of birth, date of first employment, date of leaving the company, and an estimate of the extent of hydrazine exposure based on the knowledge of the factory works manager. Each type of employment was classified in one of the following categories, according to the estimated degree of exposure.

Category 1—Exposure associated with the direct manufacture of hydrazine, or of its derivatives, or involving the use of liquid hydrazine as a raw material. Exposure to hydrazine vapour was potentially greatest for men in this category, who may have been exposed to about 1 to 10 ppm in the ambient air.

Category 2—Exposure associated with an incidental presence in an area of the plant concerned with the manufacture of hydrazine or its derivatives (fitters and engineers, for example). Exposure in this category was unlikely to have been more than 1 ppm and probably less than 0·5 or 1 ppm for most of their employment.

Category 3—Little or no exposure. Men in this category were unlikely to have been exposed to hydrazine more than slightly and then only infrequently.

The men were followed up to the end of July 1982 through the cooperation of the Office of Population Censuses and Surveys by flagging their National Health Service records in the National Health Service Central Register at Southport.

It was possible to trace 406 (95%) of the 427 men. The 21 untraced men were excluded from the study from the latest date they were known to have been living at their last known address, or, in the case of four men for whom this date was missing, from the last date of their employment in the factory. Men who changed from one category of exposure to another were considered to have been at risk in relation to the highest category to which they had previously been exposed (see footnote to table 1).

Results

Table 1 shows the number of man-years under observation according to the category of exposure, duration of exposure, and the number of years since first exposure. Nineteen per cent of the 8351 man-years at risk followed exposure in category 1.

Table 2 shows the numbers of deaths observed

Table 1 *Numbers of men exposed and man-years at risk by category of exposure, duration of exposure, and years since first exposure*

Category	*Durations of exposure*	*Years since first exposure*	*No of men*	*No of man-years*
1	6 months to 2 years	<10	78	350
		≥10	73	198
	2 years or more	<10	54	508
		≥10	50	509
	6 months or more	all	78	1565
2 or 3	6 months or more	all	375	6786
All	All	All	427*	8351

*Men who were first exposed in categories 2 or 3 and who were subsequently exposed in category 1 contributed man-years at risk in categories 2 or 3 initially and to category 1 after their first exposure in that category. The numbers of men in each category, therefore, add up to more than 427 in all, as some men contributed to more than one category. Similarly, all men who contributed man-years at risk more than 10 years after first exposure and for durations of exposure of two years or more also contributed to man-years at risk less than 10 years after first exposure and to less than two years' duration of exposure.

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Table 2 *Numbers of deaths observed and expected by category of exposure, duration of exposure, years since first exposure, and cause*

Cause of death	*Category of exposure*	*Duration of exposure*	*Years since first exposure*	*No of deaths Observed*	*Expected*
Lung cancer	1	6 months to 2 years	< 10	0	0·05
			≥ 10	1	0·10
		2 years or more	< 10	0	0·31
			≥ 10	1	1·15
		6 months or more	All	2	1·61
	2 or 3	6 months or more	All	3	5·03
	All	6 months or more	All	5	6·65
Other cancer	1	6 months to 2 years	< 10	0	0·12
			≥ 10	0	0·16
		2 years or more	< 10	0	0·42
			≥ 10	0	1·48
		6 months or more	All	0	2·18
	2 or 3	6 months or more	All	7	7·10
	All	6 months or more	All	7	9·27
Other causes	1	6 months to 2 years	< 10	0	0·60
			≥ 10	0	0·70
		2 years or more	< 10	1	2·00
			≥ 10	7	7·39
		6 months or more	All	8	10·69
	2 or 3	6 months or more	All	29	34·86
	All	6 months or more	All	37	45·55
All causes	All	6 months or more	All	49	61·47

compared with the numbers that would have been expected if the men had experienced the same death rate as those of men in the same ages in the same years in England and Wales as a whole, subdivided similarly (five year age groups and five year calendar periods). The observed mortality is close to that expected for lung cancer, other cancers, and all other causes, irrespective of the category of exposure. No deaths occurred from nasal cancer. Two men with the heaviest exposure died of lung cancer against 1·61 expected. Both had first been exposed more than 10 years before they developed the disease. One had been exposed for two months, the other for 16 years.

Discussion

The number of men exposed to hydrazine in this study is small. Only 78 men have had substantial exposure (category 1) estimated at between 1 and 10 ppm hydrazine vapour in air, and observations were made on only 707 man-years at risk for 10 years or more (up to a maximum of 36 years) after first exposure. The results obtained are encouraging in that no obvious hazard has yet appeared. They exclude, however, only gross hazards, and a note of caution is introduced by the observation of two deaths from lung cancer in men who had been first exposed in the heaviest category more than 10 years previously against 1·61 expected.

Production at this plant ceased in 1971 and the site was cleared by 1973. Some of the men were transferred to a hydrazine plant in Cheshire. This plant is completely open to the general atmosphere, and exposure levels have been low, typically 0·1 ppm. The highest recorded level has been 3 ppm, during a spillage, and such occurrences are rare. It is proposed to follow this cohort for further years.

We wish to thank Dr P Drummond and Dr A J M Slovak for the help which they gave to this study and Mr G Harmer, works manager, for his help in tracing employees and categorising them into exposure groups.

Dr Jillian Boreham is a Laing research fellow in preventive medicine.

Requests for reprints to: Professor N Wald, Department of Environmental and Preventive Medicine, Medical College of St Bartholomew's Hospital, Charterhouse Square, London EC1.

References

[1] International Agency for Research on Cancer. *The evaluation of carcinogenic risk of chemicals to man.* (IARC monograph No 4). Geneva: WHO, 1974:1–286.

[2] American Conference of Governmental Industrial Hygienists.

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Documentation of the threshold limit values. Cincinnati: ACGIH, 1980.

[3] American Conference of Governmental Industrial Hygienists. *Threshold limit values for chemical substances and physical agents in the workroom environment, with intended changes, for 1981.* Cincinnati: ACGIH, 1981.

[4] Severi L, Biancifiori C. Hepatic carcinogenesis in CBA/Cb/Se mice and Cb/Se rats by isonicotinic acid hydrazine and hydrazine sulfate. *J Natl Cancer Inst* 1968;**41**:331–40.

[5] Biancifiori C. Hepatomas in CBA/Cb/Se mice and liver lesions in golden hamsters induced by hydrazine sulfate. *J Natl Cancer Inst* 1970;**44**:943–9.

[6] Juhasz J, Balo J, Szende B. Tumour-inducing effect of hydrazine in mice. *Nature* 1966;**210**:1377.

[7] Juhasz J, Balo J, Szende B. Carcinogenic properties of hydrazine. *Magyar Onkologia* 1967;**11**:31–6.

[8] Bhide SV, D'Souza RA, Sawia MM, Ranadive AJ. Lung tumour incidence in mice treated with hydrazine sulphate. *Int J Cancer* 1976;**18**:530–5.

[9] Biancifiori C, Giornelli-Santilli FE, Milia V, Severi L. Pulmonary tumours in rats induced by oral hydrazine sulphate. *Nature* 1966;**212**:414–5.

[10] Toth B. Tumerogenesis studies with 1,2-dimethylhydrazide dihydrochloride, hydrazine sulfate, and isonicotinic acid in golden hamsters. *Cancer Res* 1972;**32**:804–7.

[11] MacEwen JD, Vernot, EH, Haun CC, Kinkead ER. *Chronic inhalation toxicity of hydrazine: oncogenic effects.* Wright-Patterson Air Force Base, Ohio 45433, USA: Air Force Aerospace Medical Research Laboratory, 1981.

[12] Roe FJC. Hydrazine. *Ann Occup Hyg* 1978;**21**:323–6.

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Toxicity Assessment of Hydrazine Fuels

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KELLER WC. *Toxicity assessment of hydrazine fuels.* Aviat. Space Environ. Med. 1988; 59(11, Suppl.):A100–6.

The major health aspects of exposure to hydrazine propellants are reviewed. Toxic effects of hydrazine fuels on humans and animals as well as *in vitro* studies are discussed with emphasis on recent findings and USAF studies. Propellant hydrazines have been found to be genotoxic in *in vitro* studies and oncogenic in animal studies. Embryotoxicity has been demonstrated at very high exposures but not at occupationally encountered levels for hydrazine and unsymmetrical dimethylhydrazine. Epidemiologic evidence to support these findings is lacking; however, the results of animal and *in vitro* studies have resulted in lowering both the time-weighted average-threshold limit values and short-term exposure limits for these propellants.

ALL METHYLATED hydrazines are substituted derivatives of the parent compound, hydrazine (H_2NNH_2). The three simple hydrazine bases, hydrazine (Hz), monomethylhydrazine (MMH), and unsymmetrical dimethylhydrazine (UDMH) are very reactive, widely used, and capable of producing a variety of toxic effects. A need for high-energy noncryogenic and storable liquid propellants which may be used in combination with other agents or as monopropellants led to the introduction of the three hydrazines as aerospace fuels. Because of the intensive use of hydrazine fuels in the aerospace industry and resultant potential exposures to personnel, the U.S. Air Force has conducted extensive toxicology studies on hydrazine fuels during the past two decades. As a result of these and other studies, the adverse effects resulting from exposure to hydrazine fuels are of significant concern. A number of comprehensive reviews of hydrazine fuel toxicology are available (1,5,8,17,21).

Recent toxicology research has been directed toward efforts to evaluate the genotoxic, oncogenic, and embryotoxic potential of hydrazine fuels for the purpose of determining safe occupational and public exposure levels. The American Conference of Governmental Industrial Hygienists (ACGIH) recommends threshold limit values (TLVs) and the National Institute of Occupational Safety and Health (NIOSH) recommends environmental exposure limits for routine occupational exposure to hydrazines (1,17); while the National Research Council Committee on Toxicology (COT) recently proposed short-term public emergency guidance levels (SPEGLs) for unusual exposures to hydrazine fuels (5).

The purpose here is to provide an overview and assessment of hydrazine propellant toxicology. Emphasis will be placed on recent developments in genotoxicity, oncogenicity, and embryotoxicity of these compounds.

Acute Toxicity Overview

The acute toxicity of hydrazine propellants is a significant operational concern. Table I compares the toxicity of hydrazine fuels by the two most likely occupational exposure routes, inhalation exposure and skin exposure. The MMH is much more toxic than either Hz or UDMH by either exposure route, with UDMH about twice as toxic as Hz by inhalation exposure, and Hz about ten times more toxic than UDMH by skin exposure.

Emergency Exposure Limits (EELs) set for the hydrazine fuels by the COT in 1974 (6) are also listed in Table I. The EEL was a ceiling limit for an unpredictable single occupational exposure, usually lasting less than 1 h, and never more than 24 h. The EELs were recommended for a narrowly defined group of aerospace workers and reflect the acceptance of the statistical likelihood of the occurrence of nonincapacitating, reversible effects in an exposed population. The EELs were not intended for application to a general industrial setting and, since they contained no safety factor, were primarily designed to avoid substantial decrements in performance during emergencies. Given the rationale behind the EELs and the historical time frame in which they were recommended, the toxicity parameters of concern would have been those associated with only

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TABLE I. ACUTE TOXICITY OF HYDRAZINE PROPELLANTS BY OCCUPATIONALLY IMPORTANT ROUTES OF EXPOSURE (6,17).

Exposure	Fuel		
	Hz	MMH	UDMH
Inhalation (ppm) (4 h LC_{50} in rat)	570	76	252
Skin ($mg \cdot kg^{-1}$) (LD_{50} in guinea pig)	93	47	1,314
1974 EEL—10 min*	30	90	100

* Inhalation exposure limit in ppm.

short-term exposures; thus, they represent an estimated acute toxicity threshold for workers. We should recall at this point in time that little data existed which suggested hydrazine propellants were oncogenic nor were significant data available concerning potential embryotoxic or genotoxic effects of hydrazine propellants.

The hydrazine fuels have a variety of effects on different organ systems (5,17). Table II summarizes the acute or short-term effects of hydrazine propellants on selected organ systems. The predominant components of hydrazine toxicity from acute or short-term exposure are respiratory irritation, liver damage, and at higher doses the central nervous system (CNS) is affected, including convulsions. The MMH is a moderate respiratory irritant which is capable of producing hyperactivity, tremors, and severe tonic-clonic convulsions from acute exposure. Aside from its convulsant activity, the most prominent features of acute or short-term MMH toxicity are methemoglobinemia, hemolytic anemia, and renal tubular damage, possibly associated with the hemolytic anemia. The UDMH is a moderate respiratory irritant which is primarily a convulsant resulting in hyperactivity, tremors, and severe tonic-clonic convulsions.

Genotoxicity of Hydrazine Propellants

Recently, the genotoxicity of hydrazine propellants has been extensively investigated. This interest in the genotoxic effects of hydrazines was stimulated by two factors: 1) publication of results of a series of studies on the oncogenic effects of various hydrazine compounds on laboratory animals; and 2) the growing body of evidence that suggests that somatic mutation may be a primary initiating factor in tumor development. Thus, hydrazines offered genetic toxicologists an opportunity to test a related series of known oncogenic compounds in proposed genotoxicity assays. Therefore, much data on the genotoxicity of hydrazine fuels were obtained as a result of investigators using these compounds to correlate the results of proposed assays for genotoxicity with the previously published results of hydrazine oncogenic studies.

Two of the more productive attempts to use short-term assays to assess hydrazine genotoxicity are those of Brusick and Matheson and Rogers and Back (3,4,20). Brusick and Matheson used a matrix of assays (Fig. 1), including microbial assays, mammalian cell culture, unscheduled deoxyribonucleic acid (DNA) synthesis, and dominant lethal assays to assess the genotoxicity of UDMH and MMH. This approach is noteworthy in that it preceded the popular strategy of matrix testing for genotoxicity. The approach was designed to allow detection of forward and reverse point mutations, chromosomal aberrations, and mitotic recombinational events induced by exposure to test substances. Neither UDMH nor MMH were mutagenic in the microbial plate assays. The UDMH had a moderately strong mutagenic effect in the mouse lymphoma assay, while MMH was negative. The UDMH also produced increased unscheduled DNA synthesis in the microsomally activated assay, while MMH was negative. Brusick and Matheson concluded from their matrix test for genotoxicity that UDMH is metabolically activated (by

TABLE II. COMPARISON OF PREDOMINANT EFFECTS ON SELECTED ORGAN SYSTEMS RESULTING FROM ACUTE OR SHORT-TERM EXPOSURE[a] TO HYDRAZINE FUELS (5,6,17).

Organ System	Fuels		
	Hz	MMH	UDMH
	Toxic effects[b]		
Respiratory (irritation)	+ + +	+	+ +
Liver (fatty change)	+ + +	+ +	+
Kidney	+ + (fatty change)	+ + + (renal tubular damage)	+
Central nervous system (convulsions)	+	+ + +	+ +
Blood	+ +	+ + + (hemolytic anemia, methemoglobinemia)	+
Skin	+ + + (necrosis)	+ + (hyperemia/edema)	+ (transient erythema)

[a] In general longer-term exposures (90 d to 1 year) or more intense exposures produce more consistent or profound nononcogenic effects than short-term or acute exposures for the same organ systems.
[b] + least, + + moderate, + + + most severely effected.

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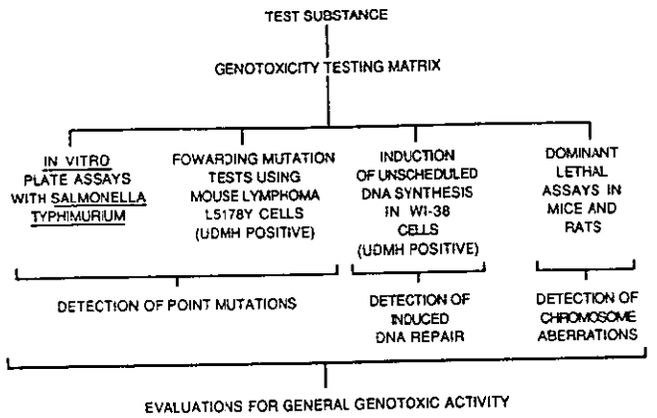
TEST SUBSTANCE
GENOTOXICITY TESTING MATRIX
IN VITRO PLATE ASSAYS WITH SALMONELLA TYPHIMURIUM
FOWARDING MUTATION TESTS USING MOUSE LYMPHOMA L5178Y CELLS (UDMH POSITIVE)
INDUCTION OF UNSCHEDULED DNA SYNTHESIS IN WI-38 CELLS (UDMH POSITIVE)
DOMINANT LETHAL ASSAYS IN MICE AND RATS
DETECTION OF POINT MUTATIONS
DETECTION OF INDUCED DNA REPAIR
DETECTION OF CHROMOSOME ABERRATIONS
EVALUATIONS FOR GENERAL GENOTOXIC ACTIVITY

Fig. 1. Composition of UDMH and MMH genetic toxicity evaluation program. MMH was negative in the matrix (3,4).

liver microsomes) to an intermediate that is genotoxic, while no conclusion could be reached for MMH.

Rogers and Back (20) used a somewhat different approach in testing the three hydrazine fuels. Instead of using a matrix of different genotoxicity assays, they used one system, the mouse lymphoma cell assay. However, four separate selective nutrient systems were used to select for mutant phenotypes arising from forward mutation. Their results correlate with those of Brusick and Matheson in that only UDMH and Hz produced mutants.

The most consistent and productive effort in investigating the basic mechanism of genotoxicity of hydrazine propellants was done by Shank and coworkers (2,13,22–24). They demonstrated the Hz but not MMH exposure resulted in substantial aberrant methylation in liver DNA. Assuming that Hz oncogenicity involves chemical alteration of DNA, DNA methylation could be a possible genotoxicity mechanism for Hz. A series of reports from this laboratory have shed light on Hz-DNA interaction, particularly within the liver. Recent findings show the alcohol dehydrogenase dependence of Hz induced DNA methylation, dose-related liver DNA methylation in chronic Hz exposures, the association between endogenous formaldehyde and Hz induced DNA methylation, the finding of even higher liver DNA methylation produced by potent liver carcinogens such as dimethylnitrosamine, and the identification of a possible intermediate, tetraformyltriazine, which is several times more potent in DNA methylation than Hz. Shank and coworkers have postulated a scheme involving the condensation of endogenous formaldehyde and exogenous Hz, resulting in formation of an electrophilic intermediate which is subsequently activated to the DNA methylating agent (Fig. 2).

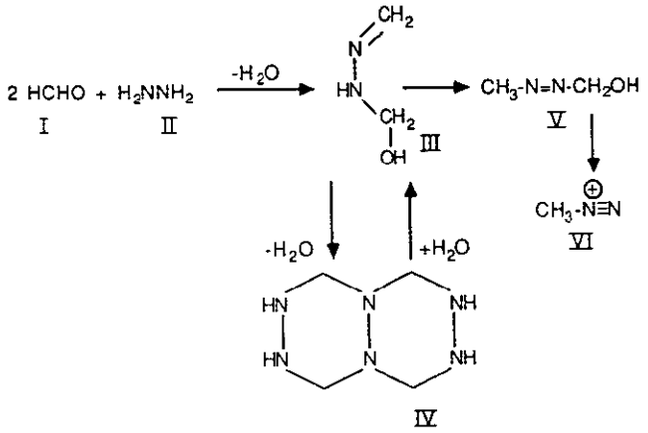

Fig. 2. Possible pathway for intracellular formation of electrophilic DNA methylating agent by condensation of Hz (II) and endogenous formaldehyde (I) which yields formaldehyde hydroxymethylhydrazone (III). Tetraformyltriazine (IV) may be an intermediate. Rearrangement could result in formation of methylazomethanol (V) which could be metabolized by alcohol dehydrogenase to methyldiazonium ion (VI), the potential electro-

When the results of these and other studies are combined, a more coherent picture of hydrazine fuel comparative genotoxicity appears (Table III). Both Hz and UDMH are generally accepted as being moderately genotoxic, with methylation of DNA as a possible mechanism of action for Hz, while MMH is generally considered to have less genotoxic potential.

Oncogenic Effects of Hydrazine Fuels

The oncogenic potential of hydrazines has been suspected for some time (17). However, in reports of epidemiologic investigations of Hz exposures, Roe (19) and more recently Wald and coworkers (25) concluded that the observed mortality from all causes, and from specific causes such as lung cancer suggested no adverse effects from Hz exposure. Wald *et al.* cautioned since the number of men studied was small, only more extreme Hz-induced effects would have been detected. No similar epidemiologic studies are available for MMH or UDMH.

Although a number of investigators have reported the oncogenicity of hydrazines in laboratory animals, the most useful studies from the standpoint of occupational toxicity assessment are the long-term inhalation studies reported by MacEwen and coworkers (9,12,16). These studies were designed to evaluate the adequacy of the occupational exposure limits. The studies included several species, and with the exception of one UDMH study, which lasted 6 months, all exposures were continued for 1 year. The exposure represented an industrial type schedule of 6 $h \cdot d^{-1}$, 5 $d \cdot week^{-1}$. Animals were maintained for at least 1 year postexposure, unless animals died or were selected for interim killing prior to the terminal killing date. A variety of exposure concentrations were used, ranging from below the TLV for

TABLE III. ASSESSMENT OF HYDRAZINE FUELS GENOTOXICITY.

Assay	UDMH	MMH	Hz
Microbial	+/−	+/−	+
Mouse lymphoma	+	−	+
Unscheduled DNA synthesis	+	−	−
Dominant lethal	−	−	−

Results compiled from Brusick and Matheson, and Rogers and Back for UDMH and MMH (3,4,20); and Epstein, Rogers and Back, and

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each fuel to 5 ppm. Table IV lists the high and low exposures for each species as well as the TLV for each fuel. The value of these studies for toxicity assessment is not only that they were well-controlled long-term inhalation studies (inhalation being the primary occupational exposure route), but that the exposure concentrations were selected to provide a range bracketing the recommended occupational exposure limits for these compounds, thus avoiding the difficulties of the high- to low-dose extrapolation process.

Results of these long-term inhalation studies revealed all three hydrazine fuels produced exposure-related tumors in a variety of organs in at least two species. Besides, the exposure-related effects were different for inhalation exposure than for the previously reported oral exposures (9,12,16,17). Significant target organs, oncogenic lesions, and other chronic lesions are listed in Table V. Emphasis was placed on tumors considered to be biologically significant. An example of this type of tumor would be the unusual malignant upper respiratory system tumors found in UDMH-exposed mice and the colon tumors found in Hz-exposed hamsters.

Chronic inhalation exposure to MMH produced lesions in all three species; however, the most susceptible species was the mouse (12). The two principal target organs were the liver and respiratory system, especially the upper respiratory system. Oncogenic findings outside these organs were limited to adenomas seen commonly in control animals. Both target organs had indications of chronic insult with inflammation, cysts and hyperplasia occurring in the upper respiratory system, and pleomorphism, bile duct hyperplasia, angiectasis, cysts, and inflammation occurring in the liver of the hamster and mouse. A significant increase in rare tumors of the upper respiratory system including papillomas, adenomas and osteomas was seen in the mouse and hamster. These benign tumors are probably also indicative of chronic insult. Lesions found in the mandibular lymph nodes of mice are also indicative of chronic inflammation of the upper respiratory system. Liver tumors included both benign and malignant types. However, these tumors occurred at significant levels only in the mouse at the highest exposure concentration, 2 ppm. From results here and other chronic studies MacEwen and coworkers classified MMH as an intermediate oncogen.

Chronic inhalation of UDMH produced lesions in two species, the mouse and the rat (9). The mouse was the more severely affected. Only benign tumors of the lung and pituitary were found in the rat. The mouse had a broad distribution of tumors; however, as with MMH, the most severely affected organs were the respiratory system and the liver. Lesions of the respiratory system included inflammation and other indications of chronic insult including a variety of rare but benign tumors of the upper respiratory system and the more common lung adenoma. Liver lesions included a variety of benign and malignant tumors similar to those seen for MMH. These lesions were seen sporadically at 0.05 ppm. From results of this study and others, MacEwen and coworkers concluded that UDMH was an intermediate oncogen.

These oncogenic findings were similar to those reported by other investigators (17); however, because of the presence of the oncogenic contaminant, dimethylnitrosamine (DMNA) in fuel grade UDMH, the etiology of tumors arising in animals exposed to UDMH was uncertain. Therefore, a follow-up study was conducted using pure UDMH. From this study, MacEwen and coworkers were able to demonstrate that other previous oncogenic findings and the findings of their study could not be explained by the DMNA contaminant.

Chronic inhalation exposure to Hz produced lesions in all three species (Table V). The rat and hamster appeared to be more severely affected; however, both species were exposed to a high dose of 5 ppm, while the mouse was exposed to only 1 ppm due to anticipated greater susceptibility to Hz (16). A significant increase in benign and malignant colon tumors and benign tumors of the upper respiratory system was seen in the hamster. The most severely affected organ system in the rat was the upper respiratory system. Lesions included inflammation and other indications of chronic insult. Both benign and malignant epithelial tumors of the nasal epithelium were found. However, these were small and could be seen only microscopically. In addition, thyroid carcinoma was found only in the male rat. Similar effects on the upper respiratory system have been found with chronic inhalation exposure of rats to formaldehyde. Since formaldehyde has a long history of use and no evidence of increased nasal cancer has been found, it is possible that the chemical irritant-associated lesions found in the rat and hamster may be associated with reactions that are characteristic of the rodent turbinate epithelium rather than with general oncogenicity of Hz or formaldehyde. Although benign tumors were found in the nasal epithelium of rats at 1 ppm, malignant tumors of the nasal region and thyroid were only found at the 5 ppm exposure level. From these results MacEwen and coworkers concluded that Hz was a relatively weak oncogen.

Thus, the long-term inhalation studies reported by MacEwen and coworkers substantiated reports of earlier studies (17), which used nonoccupationally encountered exposure routes, that long-term exposure to hydrazine fuels does produce tumors in laboratory animals. These studies also demonstrated that the upper respiratory system may be a target organ during chronic inhalation exposure. These studies also suggest these fuels are not highly potent, selective oncogenic agents, but that hydrazine fuel associated tumors, particularly those in the upper respiratory system, arise as part of a

TABLE IV. HIGHEST AND LOWEST EXPOSURE FOR EACH SPECIES AND TLV FOR EACH HYDRAZINE FUEL.

Fuel	Exposure (ppm)		TLV
	High	Low	
MMH	2^{m}, $5^{h,r}$	$0.02^{m,r}$, 0.2^{h}	0.2
UDMH	5	0.05	0.5
Hz	1^{m}, $5^{h,r}$	$0.05^{m,r}$, 0.25^{h}	0.1

Superscript on each exposure designates species: r-rat, m-mouse, h-hamster.

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TABLE V. SELECTED CHRONIC EFFECTS OF HYDRAZINE FUELS.

	Target Organs							
Fuel	Upper Respiratory System	Lung	Liver	Gastro-intestinal System	Adrenal	Thyroid	Lymphatic System	Pituitary
MMH								
Tumors	Epithelial Benign[h,m] Osteoma[m]	Adenoma[m]	Hemangioma[m] Hemangiosarcoma[m] Adenoma[m] Carcinoma[m]	Duodenal Adenoma[m]	Adenoma[h]			Adenoma[r]
Other Chronic Effects	Inflammation[h,m] Cysts[h] Hyperplasia[h]	Atelectasis[h]	Hepatitis[h] Cysts[h,m] Bile duct hyperplasia[m] Angiectasis[m] Pleomorphism[m]				Plasmacytosis[m] Hemorrhage (mandibular lymph nodes)[m]	
UDMH								
Tumors	Epithelial Benign[m] Malignant[m] Osteoma[m]	Adenoma[m,r]	Hemangioma[m] Hemangiosarcoma[m] Adenoma[m] Kupffer cell sarcoma[m]			Carcinoma[m]	Malignant lymphoma[m]	Adenoma[r]
Other Chronic Effects	Inflammation[m] Hyperplasia[m] Dysplasia[m]	Congestion[m] Perivascular cuffing[m] Lymphoid hyperplasia[m] Hyperplasia[r]	Angiectasis[m]		Amyloid-osis[h]			
Hz								
Tumors	Epithelial Benign[h,r] Malignant[r]	Adenoma[m]		Colon tumors[h]		Carcinoma[r]		
Other Chronic Effects	Hyperplasia[r] Metaplasia[r] Inflammation[r]	Epithelial hyperplasia[r]	Amyloidosis[h] Hemosiderosis[h] Bile duct hyperplasia[h,r] Cyst[h]	Colitis[h]		Amyloidosis[h]	Lymphadenitis[h] Hyperplasia[r]	

Superscript on each lesion designates species: r-rat, m-mouse, and h-hamster.

broad-based biological reaction to a long-term chemically-induced stress.

Hydrazine Fuel Embryotoxicity

The number of women in the U.S. Air Force has risen steadily in the past few years. Women currently represent about 17% of USAF recruits. The increased presence of young women in the U.S. Air Force has produced concern about the potential hazard of chemical exposure to pregnant women. No embryotoxic effects have been associated with occupational exposure to hydrazines (5,17), although a number of occupational exposures of women have been reported. A few investigators have reported the results of animal studies which evaluated the embryotoxic potential of hydrazine fuels (10,11,14,15). In one study, pregnant rats were administered 10 to 50% of an LD_{50} (intraperitoneal) of MMH or UDMH daily during the period of embryogenesis (d 6-15 of pregnancy). The results from this study indicate the embryotoxic effects of MMH and UDMH in the rat are present only at maternally toxic doses. Maternal [illegible] reduced weight gains for pregnant

maternally toxic doses. Embryotoxicity was manifested by UDMH as decreased fetal weight and possibly an increase in embryolethality and fetal abnormalities. Unfortunately no other species have been evaluated for MMH or UDMH embryotoxicity.

The embryotoxic potential of Hz has been studied more extensively than MMH or UDMH (10,14,15). Hydrazine has been evaluated in both the rat and mouse; and from occupationally important exposure routes. Initial studies in the rat were carried out similar to those described for MMH and UDMH, and indicate that Hz embryotoxicity, like that of MMH and UDMH, appears to occur only at maternally toxic doses. Just as with UDMH, this embryotoxicity is manifested as decreased fetal weight and increased embryolethality. Hydrazine embryotoxicity studies in the mouse were performed in a manner similar to the rat; however, the pregnant mice received hydrazine only during the first part of embryogenesis (d 6-9), rather than throughout the entire period of embryogenesis. In the mouse, embryotoxicity occurred at a higher dose and was manifested by the occurrence of anomalies (minor malformations) rather

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This relationship appears to hold for the embryo as well. The threshold for embryolethality in the rat is 2.5 to 5.0 $mg \cdot kg^{-1}$ while it is 20 to 30 $mg \cdot kg^{-1}$ in the mouse. This greater resistance to the embryolethal effects of Hz in the mouse may be responsible for the occurrence of anomalies as the initial indication of embryotoxicity in the mouse as opposed to the occurrence of embryolethality in the rat. Still for both species, threshold embryotoxic doses of Hz also produce maternal toxicity.

It is well known that embryotoxic agents are active during limited portions of the period of embryogenesis. Thus, it was important to determine the period of greatest susceptibility to Hz. To do this, pregnant rats were given 20% of an Hz LD_{50}, daily for 3 d, during either gestation d 7–9, 10–12, or 13–15. We determined that the initial period of embryogenesis (d 7–9) was the most susceptible period to Hz toxicity and that d 9 was the most sensitive day. Embryotoxicity was manifested primarily as embryolethality; although decreased fetal weight and a significant increase in anomalies were also observed. Maternal toxicity was again observed. The determination that a short-term Hz exposure on gestation d 9 could produce significant embryotoxicity in the developing rat embryo, coupled with reports of occupationally encountered spills and leaks of Hz, suggested the need to evaluate the effects of a single, short-term, high-level exposure such as occasionally occurs during industrial accidents. To accomplish this study, pregnant rats were exposed on gestation d 9 to either 50 $mg \cdot kg^{-1}$ or 5 $mg \cdot kg^{-1}$ of Hz by skin application for 30 min or 500 ppm or 50 ppm Hz through nose-only inhalation for 1 h. The results of this study are presented in Table VI. Both exposure routes were effective in producing embryotoxicity as manifested by embryolethality. However, it was also demonstrated that in the short-term exposure regimen, embryotoxicity also occurred only in conjunction with maternal toxicity. Thus studies in rodents, particularly the rat, suggest that Hz and possibly UDMH, are capable of producing embryotoxicity, however, this embryotoxicity occurs concurrently with maternal toxicity.

Hydrazine fuels appear to be similar to many other environmentally encountered chemicals, in that they are not selectively embryotoxic, such as the classic teratogenic drug, thalidomide, but may be capable of producing embryotoxicity at maternally toxic doses. An important distinction can be made between these two types of embryotoxic agents. A reasonable assumption of safety can be made for the embryo, for agents which are embryotoxic only at exposures which are also maternally toxic, provided occupational exposure limits are not exceeded. This assumption would not be valid for agents which are selectively embryotoxic.

Conclusion

The extensive use of hydrazine fuels within aerospace systems evoked a concurrent concern for potential toxicity resulting from occupational exposure to these fuels, and a need for an updated toxicity assessment of these fuels. A critical evaluation of the toxic effects (end points) resulting from exposure is a fundamental component of toxicity assessment. In assessing the toxicity of agents with multiple toxicity end points, such as hydrazines, all the end points must be evaluated and the most important or sensitive one identified for use in the hazard assessment process. Although the acute toxicity of hydrazine fuels was well-known a decade ago, little information was available concerning hydrazine fuel genotoxicity, potential effects of long-term inhalation exposure to low levels of hydrazine fuels, and possible embryotoxic effects of occupational hydrazine fuel exposure to pregnant women. However, as a result of recent hydrazine fuel toxicity studies, the relative importance of these end points has been determined and new, more sensitive toxicity end points have been established. These new end points have resulted in revised hazard assessments. For instance Table VII lists the COT 1974 public emergency limits (PELs), no observed effect levels for embryotoxicity (10,15), effective exposures for oncogenicity in laboratory animals (16), and the more recently established COT short-term public emergency guidance levels (SPEGLs) for hydrazine fuels. A comparison of toxicity end points is most readily done with Hz, since inhalation exposure data are available for all end points and embryotoxicity data are available from two species for Hz. Similar comparisons can be made for UDMH and MMH, although the embryotoxicity data are less extensive, and interpretation of oncogenic study results, especially for UDMH, may be more tenuous than for Hz.

It is readily apparent from comparison of the Hz data in Table VII that the effective exposure of 1 ppm for oncogenesis and >50 ppm for embryotoxicity identifies oncogenicity as the most sensitive toxicity end point. Thus, a comparison of the data in Table VII suggests that hazard assessments for Hz be based on oncogenesis. In addition, the oncogenic response occurred at a sufficiently low concentration to warrant reevaluation

TABLE VI. HYDRAZINE EMBRYOTOXICITY IN THE RAT.

	Exposure			
	High	Low (% Embryolethality)	Control	Malformations
Exposure route				
Intraperitoneal ($10 mg \cdot kg^{-1}$, days 7–9)	81	N*	N	Yes
Skin absorption, day 9 (5 and $50 mg \cdot kg^{-1}$, 0.5 h)	98	10	4	No
Inhalation, day 9 (50 and 500 ppm, 1 h)	48	3	4	N

* Not observed.

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TABLE VII. IMPACT OF TOXICITY ASSESSMENT ON RECOMMENDED EXPOSURE GUIDANCE LEVEL FOR Hz, MMH, AND UDMH.

	Exposure levels (ppm)			
	1-h PEL (1974)	Oncogenicity[a]	Embryotoxicity[b]	1-h SPEGL (1985)
Hz	10	1	50	0.12
MMH	15	2	10?	0.24
UDMH	30	0.05	30	0.24

[a] Lowest level at which oncogenic effect was seen in two species.
[b] Highest dose at which embryotoxic effect was not seen.

of the Hz exposure guidelines. Similar conclusions can be reached for the other two hydrazine fuels. Consequently, emergency guidelines from COT have been lowered. In addition, the ACGIH TLV for Hz was lowered from 1 ppm to 0.1 ppm. The studies reported by MacEwen and coworkers suggest that routine occupational exposure guidelines for MMH and UDMH should also be reevaluated.

This toxicity assessment must, however, be recognized as an interim assessment since the questions remained unanswered. Although the area of genotoxicity has experienced recent major findings, such as aberrant methylation of DNA by Hz, the significance of this finding for oncogenesis has yet to be determined; and genotoxicity assessment has yet to make a significant impact on the toxicity assessment process. In addition, the relative oncogenic potential of unusual, short-term, high-level exposure to hydrazine fuels as opposed to routine, long-term, low-level exposure to hydrazine fuels has yet to be determined. Finally, the relationship between maternal toxicity and embryotoxicity, particularly under circumstances of high-level, short-term exposures remains largely uninvestigated for hydrazines, as well as most other chemicals. Resolution of these questions may have a significant impact on future toxicity assessments of hydrazine fuels.

REFERENCES

1. American Conference of Governmental Industrial Hygienists, Committee on Threshold Limit Values. Documentation of the threshold limit values and biological exposure indices. 5th ed. Cincinnati: American Conference of Governmental Industrial Hygienists Inc., 1986.
2. Bosan WS, Lambert CE, Shank RC. The role of formaldehyde in hydrazine-induced methylation of liver DNA guanine. Carcinogenesis 1986; 1:413–8.
3. Brusick D, Matheson DW. Mutagen and oncogen study of methylhydrazine. Springfield, VA: National Technical Information Service, 1976; AMRL-TR-76-80.
4. Brusick D, Matheson DW. Mutagenic evaluation of 1,1-dimethylhydrazine, methylhydrazine, and n-phenyl-2-naphthylamine. Springfield, VA: National Technical Information Service, 1976; AMRL-TR-76-125.
5. Committee on Toxicology, Board on Toxicology and Environmental Health Hazards, Commission on Life Sciences, National Research Council. Emergency and continuous exposure guidance levels for selected airborne contaminants, Vol. 5. Washington, DC: National Academy Press, 1985.
6. Committee on Toxicology of the National Academy of Sciences, National Research Council. Guides for short-term exposures of the public to air pollutants. V. Guide for hydrazine, monomethylhydrazine, and 1,1-dimethylhydrazine. Washington, DC: National Academy of Sciences, 1974.
7. Epstein SS, Arnold E, Andrea J, Bass W, Bishop Y. Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 1972; 23:288–325.
8. Hannum JAE. Recent developments in the toxicology of propellant hydrazines. Laurel, MD: Chemical Propulsion Information Agency, Naval Plant Representative Office 1982; CPTR 82-15.
9. Haun CC, Kinkead ER, Vernot EH, Gaworski CL, MacEwen JD, Hall A, Amster RL, Bruner RH. Chronic inhalation toxicity of unsymmetrical dimethylhydrazine: oncogenic effects. Springfield, VA: National Technical Information Service 1984 AFAMRL-TR-85-020.
10. Keller WC, Olson CT, Back KC, Gaworski CL. Evaluation of the embryotoxicity of hydrazine in rats. Springfield, VA: National Technical Information Service, 1982; AFAMRL-TR-82-29.
11. Keller WC, Olson CT, Back KC. Teratogenic assessment of three methylated hydrazine derivatives in the rat. J. Toxicol. Environ. Health 1984; 13:125–31.
12. Kinkead ER, Haun CC, Vernot EH, Gaworski CL, MacEwen JD, Hall A, Amster RL, Bruner RH. A chronic inhalation toxicity study on monomethylhydrazine. Springfield, VA: National Technical Information Service, 1985; AFAMRL-TR-85-025.
13. Lambert CE, Bosan WS, Shank RC. Tetraformyltrisazine and hydrazine-induced methylation of liver DNA guanine. Carcinogenesis 1986; 7:419–22.
14. Lee SH, Aleyassine H. Hydrazine toxicity in pregnant rats. Arch. Environ. Health 1970; 21:615–9.
15. Lyng RD, Keller WC, Back KC. Effects of hydrazine on pregnant ICR mice. Springfield, VA: National Technical Information Service, 1980; AFAMRL-TR-80-19.
16. MacEwen JD, Vernot EH, Haun CC, Kinkead ER, Hall A. Chronic inhalation toxicity of hydrazine: oncogenic effects. Springfield, VA: National Technical Information Service. 1981; AAMRL-TR-81-56.
17. National Institute for Occupational Safety and Health. Criteria for a recommended standard—occupational exposure to hydrazines. Springfield, VA: National Technical Information Service 1978; 78–172.
18. Rasmussen RE. Cytologic effects of Air Force chemicals (third of a series). Springfield, VA: National Technical Information Service 1980; AFAMRL-TR-80-80.
19. Roe FJ. Letter to the editor. Ann. Occup. Hyg. 1978; 21:323–6.
20. Rogers AM, Back KC. Comparative mutagenicity of hydrazine and 3 methylated derivatives in L5178Y mouse lymphoma cells. Mutat. Res. 1981; 89:321–8.
21. Schmidt EW. Hydrazine handling. In: Schmidt EW, ed. Hydrazine and its derivatives. New York, NY: John Wiley and Sons. 1984: 454–601.
22. Shank R, Barrows WS. Alterations of DNA in hydrazine-treated rats and mice. Springfield, VA: National Technical Information Service, 1979; AMRL-TR-68.
23. Shank RC, Bosan WS, Lambert CE. Studies on the mechanism of action of hydrazine-induced methylation of DNA guanine. Springfield, VA: National Technical Information Service. 1984; AFAMRL-TR-84-057.
24. Shank RC, Bosan WS, Lambert CE. Role of formaldehyde in hydrazine-induced methylation of liver DNA guanine. Springfield, VA: National Technical Information Service, 1985; AAMRL-TR-85-052.
25. Wald N, Boreham J, Doll R, Bonsall J. Occupational exposure to hydrazine and subsequent risk of cancer. Br. J. Ind. Med. 1984; 41:31–4.

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HDMSP001793882

Service, U. S. Department of Commerce, Springfield, Virginia 22151.
25. Prough, R. A., J. A. Wittkop, and D. J. Reed. 1969. Evidence for the hepatic metabolism of some monoalkylhydrazines. *Arch. Biochem. Biophys.* 131:369-373.
26. Prough, R. A., J. A. Wittkop, and D. J. Reed. 1970. Further evidence for the nature of microsomal metabolism of procarbazine and related alkylhydrazines. *Arch. Biochem. Biophys.* 140:450-458.
27. Roberge, A., C. Gosselin, and R. Charbouneau. 1971. Effect of hydrazine on urea cycle enzymes *in vitro* and *in vivo*. *Biochem. Pharmacol.* 20:2231.
28. Roe, F. J. C., G. A. Grant, and D. M. Millican. 1967. Carcinogenicity of hydrazine and 1,1-dimethylhydrazine for mouse lung. *Nature* 216:375-376.
29. Scherfig, J., and P. S. Dixon. 1976. Use of unicellular algae for evaluation of potential aquatic contaminants. Wright-Patterson AFB, Oh. *AMRL-TR-76-65.*
30. Slonim, A. R. 1975. Behavior of hydrazine compounds in hard and soft water. Wright-Patterson AFB, Oh. *AMRL-TR-75-72.*
31. Slonim, A. R., and J. B. Gisclard. 1975. Hydrazine degradation in aquatic systems. Wright-Patterson AFB, Oh. *AMRL-TR-75-108.*
32. Slonim, A. R. 1976. Acute toxicity of hydrazine compounds to the common guppy. Wright-Patterson AFB, Oh. *AMRL-TR-76-93.*
33. Sterman, M. B. 1975. Effects of monomethylhydrazine on thalamocortical excitability of patterns of sleep in the cat. Wright-Patterson AFB, Oh. *AMRL-TR-75-34.*
34. Sterman, M. B., S. J. Goodman, and M. D. Fairchild. 1975. Effects of CNS manipulations on seizure latency following monomethylhydrazine administration in the cat. Wright-Patterson AFB, Oh. *AMRL-TR-75-80.*
35. Threshold limit values for chemical substances and physical agents in the workroom environment with intended changes for 1975. *The American Conference of Governmental Hygienists,* Cincinnati, Oh. 45201.
36. Toth, B. 1973. Tumor induction studies with substituted hydrazines. Wright-Patterson AFB, Oh. *AMRL-TR-73-125.*
37. Toth, B., and H. Shimizu. 1973. Methylhydrazine tumorigenesis in Syrian Golden Hamsters and the morphology of malignant histiocytomas. *Cancer Res.* 33:2744-2753.
38. Weinstein, R. S., and M. E. George. 1972. Interrelationship of methemoglobin, reduced glutathione and Heinz bodies in monomethylhydrazine-induced anemia. *In vitro* studies on human red cells. Proc, 3rd Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-72-130,* p 281-303.
39. Weinstein, R. S., M. E. George, and R. H. Steingart. 1975. Contribution of Heinz bodies to alterations in red cell deformability. *Tox. Appl. Pharmacol.* 32:545.
40. Wittkop, J. A., R. A. Prough, and D. J. Reed. 1969. Oxidative demethylation of N-methylhydrazine by rat liver microsomes. *Arch. Biochem. Biophys.* 134:308-315.
41. Wyrobek, A. J., and S. A. London. 1973. Effect of hydrazines on mouse sperm cells. Proc, 4th Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-73-125,* p 417-432.

Thoughts Of An Acrobatic Team Pilot

In true fighter pilot style my colleagues were strapped in and started up before I had even settled into the cockpit, but I refused to be rushed. I wanted to make sure that I was comfortable and secure before I gave the thumbs up. As we rolled onto the runway it was all becoming familiar again, just as if I had never been away, except for a slight tendency first to overcontrol. To be on the safe side, as we formed up, I eased out a bit. Although each pilot is cacooned in steel tubes and bracing wires, isolated from his colleagues yet almost near enough to reach out and touch them, he experiences a sense of unity and trust that is perhaps unique in aviation. Each man flies steadily and unwaveringly, knowing full well that his life is in the hands of the others. One is more conscious of responsibility to one's fellows than of the element of personal danger.

The Smoke Gets in Your Eyes. Neil Williams *Shell Aviation News,* No. 441:2-7, 1977

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Occupational Hazards of Missile Operations With Special Regard to the Hydrazine Propellants

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BACK, K. C., V. L. CARTER, JR., and A. A. THOMAS. *Occupational hazards of missile operations with special regard to the hydrazine propellants.* Aviat. Space Environ. Med. 49(4):591-598, 1978.

The second generation of ballistic missiles and boosters, characterized by increased range and quick reaction capability, required the development of new high-energy storage propellants. This exploration led to the introduction of hydrazine (Hz), monomethylhydrazine (MMH), and 1,1-dimethylhydrazine (UDMH) into the USAF inventory. These compounds are all storable, noncryogenic, high-energy fuels which may be used alone or in combination as mixed amine fuels. Early toxicology experiments were to produce data on acute and subacute effects of the propellants in order to set standards for test and operational procedures to protect propellant handlers. The early work indicated that, despite similar chemical characteristics, there were marked differences between the compounds in terms of toxicological mechanisms. Since the propellant systems have been used for some 15 years, recent emphasis on toxicology has been centered on the more chronic effects and on an increasing body of evidence from animal experiments that the compounds may possess oncogenic potential as well as chronic systemic effects. This paper addresses itself to data leading up to current occupational standards.

THE SECOND GENERATION of ballistic missiles and boosters, characterized by increased range and quick reaction capability, required the development of new high-energy storable propellants. This exploration led to the introduction of hydrazine (Hz), monomethylhydrazine (MMH), and 1,1-dimethylhydrazine (UDMH) into the United States Air Force inventory. These compounds are all storable, noncryogenic, high-energy fuels which may be used alone or in combination as mixed amine fuels. Further, hydrazine and its derivatives are finding increasing commercial application as intermediates in the synthesis of other products. Hence, substantial quantities of these agents are presently manufactured, stored, and shipped in the USA. The materials are all quite toxic and present a potential hazard to personnel who handle or are in contact with them under any and all use conditions. In addition, they may pose a hazard to the general population, if accidentally released into the general environment, as a result of missile malfunction or transportation mishap. Consequently, propellant toxicology has become one of the major areas for USAF research in toxicology. Early work was designed to produce data on the acute and subacute effects of the propellants in order to set standards for test and operational procedures to protect propellant handlers. The early work indicated that, despite similar chemical characteristics, there were marked differences between the compounds in terms of toxicological mechanisms. All of the compounds produce different levels of central nervous system irritation (convulsions) as well as eye, skin, and respiratory tract irritation. The magnitude of these effects varies widely among the three, and two have rather unique actions. Hydrazine can cause hemolytic effects in man and animals. Experimental studies have indicated that the convulsant action of UDMH and MMH can be aborted by the use of Vitamin B6, though the agent is ineffective against hydrazine toxicity. Since the propellants and some systems have been in use for about 15 years, the emphasis on toxicology has been centered on the more chronic effects. Of further concern is an increasing body of evidence from some animal experiments that hydrazine and some of its derivatives as well as MMH and UDMH, may possess oncogenic potential as well as chronic systemic effects. Further, some manufacturing processes for MMH and UDMH require the use of an oncogenic compound, N-nitrosodimethylamine, which may remain as a trace contaminant. With the advent of new occupational safety and health standards required for potential carcinogens advocated by the Environmental Protection Agency and the Occupational Safety and Health Administration, it has become mandatory to produce data which can be useful in the evaluation of oncogenic potential for the hydrazines. This presentation will address itself to data leading up to present standards, such as the Threshold

The experiments reported herein were conducted according to the "Guide for the Care and Use of Laboratory Animals," DHEW 73-33.

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Limit Value, Emergency Tolerance Criteria, Criteria for Short-Term Exposure to the Public, and oncogenic potential of these hydrazines.

The recent rapid advances in aerospace technology have brought about an increasingly complex chemical environment in which man must operate effectively in the research laboratory, in the giant governmental and industrial field complex, and in the relatively new environments of space and deepest oceans. Chemists and materials engineers are spawning new chemicals and new uses for old chemicals at a rate infinitely faster than toxicologists, pharmacologists, and industrial hygiene and industrial medicine personnel can cope with the many-faceted problems presented by these compounds. The second generation of ballistic missiles and boosters, characterized by increased range and quick-reaction capability, required the development of new high-energy storable propellants. The Department of Defense, the National Aeronautics and Space Administration, and the Federal Aviation Agency, as well as many private and industrial concerns, have been instrumental in sponsoring a great deal of research in the areas of propellants, fuels, oxidizers, and other chemicals. Unfortunately, the price for increased energy content has been increased reactivity and biological activity. Consequently, propellant toxicology has become one of the major areas for United States Air Force (USAF) research. To understand and properly evaluate the health hazards peculiar to a certain propellant or, indeed, any chemical compound, its pharmacological properties must be investigated, the pathways of metabolism, absorption, distribution, excretion, and the type and magnitude of pathology must be established, and diagnostic and therapeutic methodology must be developed. Based on these factors, tolerance criteria can be recommended for personnel who are in contact with these compounds under any and all use conditions.

Another major area of research concerns environmental pollution that results from large-scale and extended propellant and motor test operations. In this instance, other byproducts of propellant usage become increasingly important. Combustion products, motor exhausts, chemically treated wastes, and products reacting with the environment possess potential toxicity to animal and human life, vegetation, and soil microflora. The most important potential problem is pollution of community air and water around large-scale industrial research and development operations. The sources for such pollution are either acute (large spills, transportation accidents, waste disposal, test firing of motors) or cumulative (venting and flare-off of propellant vapors, routine decontamination procedures, long term operations). Evaluation of the environmental pollution profile of a specific propellant operation requires both controlled experimental laboratory studies and on-site field investigations using mobile analytical laboratories.

Two major problem areas are peculiar to aerospace operations. The first is the type of exposure that is usually encountered by USAF personnel. Contrary to the industrial type of exposure during the production of propellants, where frequent daily low-level exposure occurs and industrial Threshold Limit Values (TLV) are applicable for protective purposes, most of the field operations are characterized by infrequent short-duration, high-level exposures that are generated by test activities or by accidental release of propellants. Under the latter circumstances, TLVs are meaningless and become extremely difficult to live with. In the past few years, much research effort has been expended in characterizing tolerance to high-level, short-duration exposure, and in establishing Emergency Exposure Limits (EEL) for missile operators.

The establishment of scientifically valid and safe EELs requires extensive animal experimentation, highly specialized inhalation facilities, and the application of psychopharmacological principles in addition to the classical pharmacological and toxicological methods. The philosophy of emergency exposure is predicated on three cardinal assumptions: a) nobody will be intentionally exposed to high concentrations of propellant vapors under ordinary circumstances; b) if exposed, subjective and objective symptomatology may occur but pathology should be reversible; and c) while discomfort and pathology are tolerable, performance of the operator must not be impaired. On the basis of animal and any human exposure data available, EELs are recommended by either the American Conference of Governmental Industrial Hygienists or by the Committee on Toxicology, National Research Council, National Academy of Sciences.

Of course, in the establishment of the TLV or EEL increasing emphasis has been placed on the possibility that a compound may possess teratogenic, mutagenic, or oncogenic potential. A large amount of very expensive and time-consuming effort is being expended in this regard.

Inasmuch as the literature is quite voluminous concerning the toxicology and pharmacology of the propellant hydrazines, this paper will deal only with pertinent information published since 1970. For details of earlier data one is referred to two comprehensive review articles (2,3). The most recent review of health hazards from hydrazine (Hz), monomethylhydrazine (MMH), and 1,1-dimethylhydrazine (UDMH) was accomplished by the Committee on Toxicology, National Research Council, National Academy of Sciences, and published in June 1974 (24). We are in complete agreement with the findings and interpretations in this document, which very adequately covered animal toxicity data; absorption, distribution, and excretion; effects on metabolism and enzymes; target organ effects and tissue pathology; carcinogenicity and mutagenicity; human health effects and therapy of intoxication. The document also contains an extensive and excellent list of references from the United States and world scientific literature.

NEW TOXICOLOGY DEVELOPMENTS

The most significant impact of the recently completed and currently ongoing research is in the area of safety margin for Threshold Limit Values (TLV) and oncogenic potential of the three hydrazine propellants:

a) The safety margin for the hydrazine TLV wa

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tested by inhalation exposures in animals and was found nonexistent (12,20). As a result, the TLV committee has already tentatively lowered the hydrazine TLV from 1.0 ppm to 0.1 ppm in the 1975 pamphlet under "Notice of Intended Changes." Although our referenced experiments were not designed as oncogenic studies, mice kept for 1 year postexposure observation have shown a dose-dependent increase in alveolargenic carcinomas compared to controls. This finding, coupled with other reports from the literature (feeding studies), has also placed hydrazine on the A2 list of "Occupational Substances Suspect of Oncogenic Potential for Workers" (35).

b) UDMH has also been implicated to be tumorigenic by oral administration in drinking water in the mouse (28,36) but not in the rat (1), and no long-term inhalation exposure studies were done.

c) MMH has been similarly implicated to be tumorigenic in the hamster (36,37) when ingested in drinking water; however, a recently completed similar study using hamsters in our laboratories (22) failed to confirm the high incidence (43%) of Kupffer cell sarcomas observed by Toth.

d) There are no known cancer cases among hydrazine, MMH, and UDMH propellant manufacturing and handling personnel as of today.

Because of the demonstrated oncogenic potential of all three hydrazine propellants in either the mouse or the hamster, but not in the rat, by the oral route in studies completed elsewhere, our observations on hydrazine-exposed mice by the inhalatory route, and the recommendation of the Committee on Toxicology, National Research Council, National Academy of Sciences report (24) that "additional research on the potential carcinogenicity of these compounds should be conducted," definitive oncogenic dose-response studies have been initiated in our inhalation exposure facilities using large numbers of mice, rats, and hamsters, and a limited number of dogs, as biochemical indicators. The UDMH and hydrazine exposures have been completed, and MMH exposures initiated.

Effects on Animals

1. *Acute Toxicity*:

a) Hydrazine (Hz), Monomethylhydrazine (MMH), and Unsymmetrical Dimethylhydrazine (UDMH).

Darmer and MacEwen exposed dogs, monkeys, and rats by inhalation to 1 ppm MMH for 24 h (4). No adverse effects were observed during the exposure, in the clinical chemistries obtained biweekly during the 30-d postexposure period, nor in histopathological examination of the animals 30-d postexposure.

In preparation for the use of hamsters as one of the test species in oncogenic studies of the propellant Hz, inhalation studies were performed to determine the acute lethality to this species. MacEwen and Vernot (21) established the 1-h LC_{50}'s for MMH, UDMH, and Hz as 991 ppm, 2271 ppm, and 2585 ppm, respectively. All three compounds caused severe respiratory irritation and central nervous system effects. Convulsions were produced after exposure to MMH and UDMH but not following exposure to Hz vapors. However, exposure Hz vapors, regardless of concentration, resulted in s vere hair loss to hamsters. All three compounds caus significant lung, liver, and kidney damage, even at t lowest levels tested in this study. These results indica that although the hamster is less susceptible than the r or the mouse, it reacts to toxic levels of these three cor pounds in a similar manner to that reported for oth species.

2. *Repeated Dose Toxicity*:

a) Monomethylhydrazine (MMH).

In an effort to determine a true no-effect level f chronic exposure to MMH, Darmer and MacEwen co ducted continuous 90-d inhalation studies on dog monkeys, and rats (4). At 0.1 ppm, rat growth rat were significantly reduced although organ weights ar organ-to-body weight ratios were not significantly a tered. The dogs demonstrated significant increases i serum phosphorus and alkaline phosphatase values a this exposure level and were the only species to demor strate gross pathologic changes characterized by nutme appearing livers. No adverse effects attributable to e posure were seen in the 0.04 ppm-exposed animal This study complemented a previous study by Hau (11) where dose-related toxic responses were observe in dogs, monkeys, rats, and mice exposed to 2 and ppm MMH intermittently for 6 months.

b) Hydrazine (Hz).

Results of 6-month intermittent and continuous H inhalation exposures to mice, rats, dogs, and monkey were reported by Haun and Kinkead (12) and Mac Ewen *et al.* (20). The doses selected for the intermitter (industrial regimen) study were 5 and 1 ppm, the latte being the current TLV at that time. Doses for continuou exposure were 1.0 and 0.2 ppm, which approximatel equalled the CT (concentration × time) values for th intermittent study. The hepatotoxic response in mice an the weight loss and anemia seen in the dogs resultin from exposure to the lower doses indicated that the 1.(ppm TLV may be too high. A small group of mice wa held for 1 year postexposure observation. Although th small number of animals precluded any statistical eval uation, the increased dose-related incidence of alveo largenic carcinomas occurring in these mice suggestec that an oncogenic problem may be associated with chron ic inhalation exposures to this compound (20).

c) Unsymmetrical Dimethylhydrazine (UDMH).

As previously stated, inhalation studies to determine the oncogenic potential of these hydrazine propellants are underway. Although, at the time of manuscrip preparation, the oncogenic portion of these studies was incomplete, certain salient observations on UDMH toxicity from this study are worthy of note.

Animals used in this study consisted of 400 female C57 black mice, 200 male CDF (Fischer 344 derived) albino rats, 200 male Engle Golden Syrian hamsters, and four male and four female beagle dogs per group. A separate set of control animals was provided for the 0.05 ppm test since it was not started at the same time as 5 ppm and 0.5 ppm experiments. Two chambers were used for each UDMH air concentration. Each pair of

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chambers contained as few species as possible to minimize the risk of cross infection. Dogs and rats were housed in one dome and mice and hamsters in the companion chamber. All control animals were maintained in animal holding facilities.

The Thomas Domes in the Toxic Hazards Research Unit (THRU) were operated with nominal airflows of 35 ft^3/min at a slightly reduced pressure of 725 mm Hg to prevent leakage of UDMH into the laboratory. Exposures were conducted on a 6 h/d, 5 d/week schedule. No exposures were made on weekends and holidays.

Overt signs of UDMH toxicity were nonexistent in animals exposed for 6 months to 5 and 0.5 ppm UDMH. Growth curves for both groups of dogs and mice were normal compared to those of the control groups. In the case of the rats, however, statistically significant lower weight-gain rates were noted for both exposed groups throughout the 6 months of exposure. Hamster weights were somewhat erratic and showed no gain when mean weights at exposure conclusion were compared with initial weights. Their mean weights with one exception (the 5 ppm-exposed group at 4 weeks of exposure) were significantly lower than control during the entire exposure period. Effects on the weight of exposed rats or hamsters were not dose-dependent.

Results of clinical chemistry tests made on dogs biweekly during and following exposure were all normal except for serum glutamic pyruvic transaminase (SGPT) values. The SGPT values were significantly elevated in dogs exposed to 5.0 ppm UDMH after the first biweekly sampling period. A sharp reduction, approximately 50%, occurred at 2 and 4 weeks postexposure. Recovery was complete by 6 months postexposure.

Special liver function tests were performed on dogs at exposure termination. Prothrombin time and cephalin flocculation values were normal but bromsulphalein (BSP) measured in the blood of the 5-ppm exposed dogs 10 min following 10 mg/kg injection showed significant retention. This test was repeated at 4 weeks postexposure with similar results. However, BSP values all returned to normal 9 months postexposure.

These data indicate that significant exposure effects of UDMH were limited to slight-to-moderate hepatotoxicity in dogs exposed to the 5 ppm concentration with recovery 6 months postexposure. No toxic effects were observed in the 6 month 0.5-ppm or 0.05-ppm exposed animals. On the basis of results of tests and measurements used in this study, the current industrial TLV of 0.5 ppm UDMH appears to be well chosen without consideration of cancer risk. Cancer incidence will be assessed during the lifetime observation and testing of the rodents and dogs. Details are found in previous reports (11,20,23).

3. *Effects on Metabolism and Enzymes*:

a) Hydrazine (Hz), Monomethylhydrazine (MMH), and Unsymmetrical Dimethylhydrazine (UDMH).

Dost, using radiorespirometric techniques, reported that subacute exposure to MMH causes a hyperglycemic response in intact animals which results from an interference with glycolysis in the hexose phase of anaerobic glycolysis. Glucokinase, hexokinase, and pyruvate kina are all inhibited by MMH but the major inhibitory effe appears to be the phosphofructokinase step. Conversely Hz produces a hypoglycemic response and Dost reporte that the probable site of action occurs after pyruva decarboxylation with an interference in the flux of th acetate fragment into fatty acid synthesis and eventu oxidation. Dost also confirms the inhibition of glycoge synthesis by Hz and indicates that the site of interferenc occurs after glucose-6-phosphate formation (6).

These effects of MMH and Hz on glucose metabolism appear dose- and time-related; these studies represen high doses, 0.5-1.0 acute LD_{50} given over periods of several hours to healthy normal animals. The effects were not observed at lower doses, although the changes in glycolysis were evident when only part of the total dose was received.

Dost also reported MMH and Hz cause a decrease in methylamine and putrescine oxidation, confirming previous work. MMH was more effective than Hz and methylamine oxidation was more sensitvie to the inhibition by the Hz than putrescine.

In 1969-70, Prough, Wittkop, and Reed (25,26,40) reported the presence of microsomal enzyme systems in rat liver capable of metabolizing MMH and UDMH. Two modes of metabolism were noted: an alkylhydrazine oxidase converting alkylhydrazines to corresponding alkanes and an N-methylhydrazine demethylase producing formaldehyde from the n-methyl group. These two systems were found, singly or together in varying degrees of activity in several animal species. Studies were done to determine the relationship of these enzyme systems to microsomal redox components cytochrome b_5 and P450. The oxidase activity is not dependent on P450 and cannot be induced by phenobarbital or 3-methylcholanthrene. However, there appear to be two demethylase enzyme systems present in rat liver microsomes, one inducible and dependent on P450 and one not, both capable of demethylating N-methylhydrazines. Kato *et al.* (18) also reported that MMH and UDMH can inhibit activity of drug-metabolizing enzymes in liver microsomes and suggested their effectiveness of inhibition is related to the degree of lipid solubility of the individual hydrazines. Roberge *et al.* (27) investigated the effect of Hz on urea cycle enzymes *in vitro* and *in vivo*. Ornithine keto-acid transaminase was inhibited provoking accumulation of ornithine. The high concentration of ornithine and increased ammonia production stimulates urea synthesis. The condensation reaction of citrulline and aspartic acid is rate-limiting for the urea cycle with resultant accumulation of citrulline.

Hawks *et al.* (13) reported no inhibition of incorporation of amino acids into rat liver protein by UDMH or MMH.

Dost *et al.* (5) reported Hz causes a two-fold increase in brain Gamma Aminobutyric Acid (GABA) as the inhibition of GABA transaminase was higher than the interference in GABA formation by decarboxylation of glutamic acid. MMH also strongly inhibits GABA transaminase whereas UDMH has only a moderate in-

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[redacted]ycogenic potential of MMH to hamsters when administered in drinking water. Thirty hamsters received 0.01% of MMH in drinking water adjusted to pH 3.5 with HCl; 30 hamsters received 0.01% MMH in drinking water not pH controlled; 17 hamsters served as controls. The study was conducted for the life of the hamsters beginning at 5 months of age. No significant increase in tumor incidence attributable to the MMH could be determined.

5. *Mutagenesis*:

a) Hydrazine (Hz), Monomethylhydrazine (MMH), and Unsymmetrical Dimethylhydrazine (UDMH).

Wyrobek and London (41) utilizing an *in vivo* mammalian test system, involving examination of murine spermatogenesis, evaluated the mutagenic potential of Hz, MMH, and UDMH. Groups of mice received doses of each coupound ranging from 0.1-0.9 of the LD_{50} for 5 d. They established both a dose and a dose-time relationship between injection of these compounds and the appearance of abnormal sperm.

6. *Effects on Behavior*:

a) Monomethylhydrazine (MMH).

Sterman (33) conducted studies on the behavioral effects of MMH in the cat. The influence of subconvulsive exposure was examined with reference to a more basic aspect of physiological function than previous sensorimotor and performance studies; namely, the organization of sleep-waking patterns. Polygraphic recording providing for classification of states of sleep and wakefulness were obtained over a 10-h period following either saline or MMH (5 mg/kg, IP) injections. MMH caused no overt behavioral disruption on transient observation at this dosage; however, analysis of polygraphic data disclosed a significant depression of sleep and disruption of normal diurnal rhythms. Sleep suppression lasted approximately 6 h and was followed by a profound sleep rebound. The behavioral effects of MMH exposure extended beyond the realm of sensorimotor functions. The influence noted upon sleep could have equally serious and different consequences in performance. The effect of MMH upon thalamocortical conduction was also examined. Cats were operantly trained to suppress movement by rewarding a sensorimotor EEG rhythm, the SMR, with positive hypothalamic brain stimulation. Other cats received similar, but non-contingent, reward. Following training, the two groups were administered MMH (10 mg/kg, IP) and thalamically induced somatosensory-evoked potential responses measured until seizures occurred. The non-contingent group showed an expected increment in response prior to seizures, while the SMR-trained cats showed a decrement or reduced increment. Sterman *et al.* (34) investigated the influence of intracranial electrode placement upon the seizure response to MMH. Efforts were also made to replicate previous findings with regard to the effects of EEG operant conditioning on this response. Thirty cats were studied, 10 in each of imental groups were: 1) an unoperated group, 2) an operated group with cortical and subcortical electrodes, and 3) an operated group as in 2), but provided additionally with sensorimotor rhythm (SMR) EEG operant conditioning. The operated group without EEG conditioning showed a significantly reduced and more stable latency to seizures when compared to the other two groups. These findings suggested that 1) some aspect of the procedure associated with central nervous system electrode implantation increased susceptibility to MMH-induced seizures, 2) unoperated animals had individual differences in seizure susceptibility, but were significantly more resistant to MMH toxicity than operated animals, and 3) SMR-trained operated animals had individual differences in response to training, but were also more resistant to MMH toxicity.

Effects on Humans

1. *Monomethylhydrazine (MMH)*:

The hemolytic response observed in dogs and the documented Heinz body formation in humans following acute MMH exposure led Weinstein and George (38) and George (7) to study the *in vitro* response of human red blood cells to MMH. These initial studies led to a preliminary conclusion that the hemolytic effect of MMH observed *in vivo* is caused either by a direct action of this oxidant on cell membrane, which is not obvious on fixed morphological observation, or by the effect of Heinz bodies on cellular integrity leading to a decreased cellular "deformability" and premature removal of the injured cells from the circulation by the spleen, or both. Later studies by George (8), designed to measure direct effects of MMH on compartments of cell membranes, potassium flux, autoxidation of membrane lipids, and alteration of membrane protein, gave additional support to the thesis that the major mechanism of red cell destruction following exposure to MMH appears to be the physical presence of Heinz bodies in the red cell, resulting in a decreased deformability of the cell and accelerated sequestration and destruction by the spleen. Studies also indicated that any enzyme deficiencies, such as lack of glucose-6-phosphate dehydrogenase, 6-phosphogluconic dehydrogenase, or glutathione reductase (which affects 2-10% of black males and 0.3% white males) would exaggerate hemolysis and prevent reversal of the response. Personnel with this sort of genetic red cell disease should not be exposed to MMH, even though minimal. Weinstein *et al.* (39) compared morphologically the Heinz bodies formed by MMH and acetylphenylhydrazine (APH) and studied the relationship between these Heinz bodies and red blood cell deformability. Unlike APH-induced Heinz bodies, MMH-induced Heinz bodies show little affinity for the cell membrane and are free of the membrane when decreases in deformability are first detected. These results show that alterations in red cell deformability with oxidative injury may

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be unrelated to Heinz body-cell membrane interactions. Ultrastructural observations suggest that denatured hemoglobin diffusely distributed in the cytoplasm may polymerize into a loose network and account for the altered rheological properties of MMH-injured red cells.

Effects on Non-mammalian Life Forms

1. Aerozine 50 (Az-50), a 50/50 mixture of Hz and UDMH, Hydrazine (Hz), Monomethylhydrazine (MMH), and Unsymmetrical Dimethylhydrazine (UDMH).

Hoover *et al.* (17) related aquatic decomposition rates of Hz and UDMH to the presence of oxygen, the presence of a catalyst such as copper, to water temperature, and to water pH. These studies were expanded by Gormley and Ford (9) to include MMH. Based upon a stoichiometric relationship between the amount of propellant degraded and the amount of dissolved oxygen (D.O.) in the water, first-order rate constants were developed for copper catalyzed degradation of these propellants. Lurker (19) has used similar methodology to study in more detail the effect of other ions present in water and to better define the effect of temperature on degradation rates. Slonim (30) studied the effects of Hz, UDMH, Az-50, and MMH when placed in hard and soft water over a 96-h period. At 100 mg/l but not at 1 mg/l, the hydrazine produced a transitory drop in the D.O. of hard water. The effects were not seen in soft water. Slonim and Gisclard (31) also developed a rapid and sensitive polarographic method for measuring Hz in solution. The method was used to study the stability or degradation of Hz over a 96-h period in river, lake, pond, county, city, and laboratory water. Varying amounts of degradation of Hz were observed in many of these waters. Hz was relatively stable in soft water and softened city water.

Heck *et al.* (14) exposed goldfish, daphnia, and dragonfly nymphs to Hz and UDMH during static, unreplenished bioassays. The 48-h Hz LC_{50} values were 3.2, 2.4, and 320 mg/l, respectively. Natural pond water was the dilution water used. The UDMH was found to be about one-tenth as toxic since it produced 48-h LC_{50} values of 32 mg/l for the goldfish and 24 mg/l for the daphnia. Heck *et al.* (15), in similar static bioassays, extended their studies to include goldfish, green sunfish, small bluegill, large bluegill, channel catfish, and largemouth bass, using dilution water containing 0.15 mg/l copper. The 48-h LC_{50} for Hz varied from a low of 1.6 mg/l in the catfish to a high of 5.2 mg/l in the large bluegill. The 48-hour LC_{50}s for UDMH were much higher, ranging from 16.5 mg/l for small bluegill to 58 mg/l in goldfish.

Hoover *et al.* (17) performed static bioassays using goldfish, catfish, bass, and daphnia to study the toxicity of Hz and UDMH in "copper free" (<0.01 mg/l Cu^{II}) water. His results were not significantly different from those produced by the low copper concentrations in Heck's dilution water.

Heinemann and Rose (16) conducted bioassays using two marine species to determine the toxicity of Az-50. The 72-h LC_{50} for sheepshead minnows was 5.1 mg/l. For grass shrimp the 72-h LC_{50} was 0.78 mg/l.

Slonim (32) compared the toxicities of Hz, UDMH, MMH, and Az-50 to guppies in hard and soft water. With the exception of UDMH, all were more toxic in soft than in hard water. The LC_{50} values ranged from 0.6 mg/l for Hz in soft water to 26.5 mg/l for UDMH in soft water.

Greenhouse (10) studied the effects of Hz, MMH, and UDMH on amphibian embryos and larvae. He used the South African clawed toad, *Xenopus laevis*. Hz was not acutely toxic to post-hatching larvae in concentrations up to 400 mg/l. However, Hz is teratogenic at 40 mg/l if exposure occurs prior to the completion of neurulation. UDMH at 10 mg/l was teratogenic to all embryonic stages whereas 100 mg/l was lethal.

The effect of these propellants has also been studied in aquatic plants. Heck *et al.* (15) grew *Chlorella* in varying concentrations of Hz and UDMH to observe the effects on growth. Concentrations of 1, 10, and 100 mg/l were compared with the controls. All concentrations of Hz had an inhibitory effect with the 100 mg/l concentration producing a complete cessation of growth. The 1 and 10 mg/l concentrations of UDMH had little effect while the 100 mg/l produced some inhibition. Sherfig *et al.* (29) studied the effects of Hz and UDMH on the growth of *Selenastrum capricornutum*. Hz in concentrations of 10 μl/l produced an algal cell volume growth of only 14% of the control growth. UDMH at 10 μl/l reduced the growth of algae to about one-half of the growth of the controls. In contrast, the addition of low levels of UDMH (1 μl/l) resulted in an increase in algal growth which was probably the result of a nutrient effect. Hz appears to be much more toxic by inhibiting growth of the test algae than UDMH.

1. *Airborne Concentrations/Acute Exposures:*

a. Military and Space Operations

EMERGENCY EXPOSURE LIMITS (EEL)

	10 Min	30 Min	60 Min	24 H
Hydrazine	30 ppm	20 ppm	10 ppm	—
Monomethyl-hydrazine	90 ppm	30 ppm	15 ppm	1 ppm
1,1-Dimethyl-hydrazine	100 ppm	50 ppm	30 ppm	—

b. Industrial and Production Plants

SHORT-TERM PUBLIC LIMITS (STPL)

	10 Min	30 Min	60 Min
Hydrazine	15 ppm	10 ppm	5 ppm
Monomethylhydrazine	9 ppm	3 ppm	1.5 ppm
1,1-Dimethylhydrazine	50 ppm	25 ppm	15 ppm

PUBLIC EMERGENCY LIMITS (PEL)

	10 Min	30 Min	60 Min
Hydrazine	30 ppm	20 ppm	10 ppm
Monomethylhydrazine	90 ppm	30 ppm	15 ppm
1,1-Dimethylhydrazine	100 ppm	50 ppm	30 ppm

2. *Airborne Concentrations/Chronic Exposures:*

OCCUPATIONAL THRESHOLD LIMIT VALUES (TLV)

Hydrazine*	0.1 ppm	"Skin"

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Monomethylhydrazine	0.2 ppm	"Skin"
1,1-Dimethylhydrazine	0.5 ppm	"Skin"

* Suspect carcinogen.

3. *Direct Contact*:

a) All three propellant hydrazines penetrate the eye and the skin readily if not immediately flushed away with copious amounts of water for 15 min. Failure to promptly remove the chemical may result in systemic toxicity.

b) Always wear approved protective equipment to avoid direct contact.

4. *Biologic Standards*:

a) For occupational (at the TLV level) exposures, there are no biological indicators, such as blood or urinary levels of the hydrazines or their metabolites that could be used at the present for monitoring the workers who are *not* suffering ill effects. Because of the relatively fast clearance rate of hydrazines from the body, no accumulation of the propellants or their metabolites is expected within the detectable range using current techniques and analytical procedures suitable for monitoring the working population.

b) In acute exposures at the EEL levels, monomethylhydrazine can cause Heinz body formation in the red blood cells, up to 5% after 7 d postexposure to 90 ppm for 10 min. Under these circumstances there is no measurable methemoglobin formation and, hence, the exposure is not considered to be of medical consequence.

5. *Engineering Controls/Personal Protection*:

For handling propellant hydrazines, one should consult Department of the Air Force Manual, Volume II, AFM 161-30, titled "Aerospace Medicine: Chemical Rocket/Propellant Hazards," dated 10 April, 1973.

6. *Medical Examination of Workers/Preemployment and Annual*:

a) Complete physical examination (Class III Flight Physical).

b) Laboratory tests should include pulmonary function and chest X-ray, hematology, liver function, kidney function, and EEG.

c) Contraindications for working with hydrazine propellants should include pregnancy, anemias and hematologic disorders, history of convulsive episodes and other neurologic disorders, "slow acetylators", glucose-6-phosphate dehydrogenase deficiency, 6-phosphogluconic dehydrogenase deficiency, glutathione reductase deficiency, therapeutic use of tranquilizers, and the existence of "benign" tumors.

REFERENCES

1. Argus, M. F., and C. Hoch-Ligeti. 1961. Comparative Study of the Carcinogenicity of nitrosamines. *Natl. Cancer Inst. J.* 27:695-709.
2. Back, K. C., and A. A. Thomas. 1970. Aerospace problems in pharmacology and toxicology. *Ann. Rev. Pharmacol.* 10:395-412.
3. Clark, D. A., J. D. Bairrington, J. L. Bitter, F. L. Coe, M. A. Medina, J. H. Merritt, and W. N. Scott. 1968. Pharmacology and toxicology of propellant hydrazines. USAF School of Aerospace Medicine, Brooks AFB, Tx. *Aeromedical Review 11-68.*
4. Darmer, K. I., Jr. and J. D. MacEwen. 1973. Monomethylhydrazine—chronic low level exposures and 24-hour emergency exposure limits. Proc, 4th Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-73-125,* pp. 373-387.
5. Dost, F. N., D. J. Reed, and C. H. Wang. 1971. Effects of various hydrazines on metabolism of GABA-1-^{14}C in rats. *Biochem. Pharmacol.* 20:1702.
6. Dost, F. 1975. Metabolic effects of simple hydrazine compounds. Proc, 6th Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-75-125,* pp. 257-273.
7. George, M. E. 1973. Effects of monomethylhydrazine on human red blood cells. Wright-Patterson AFB, Oh. *AMRL-TR-73-26.*
8. George, M. E. 1974. Effects of monomethylhydrazine on red blood cell metabolism. Wright-Patterson AFB, Oh. *AMRL-TR-74-87.*
9. Gormley, W. T., and R. E. Ford. 1973. Deoxygenation of environmental waters by hydrazine-type fuels. Proc, 4th Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-73-125,* p 387-401.
10. Greenhouse, G. 1976. Effects of pollutants on eggs, embryos and larvae of amphibian species. Wright-Patterson AFB, Oh. *AMRL-TR-76-31.*
11. Haun, C. C. 1970. Chronic exposure to low concentrations of monomethylhydrazine. Proc, 1st Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-70-102,* p. 341-355.
12. Haun, C. C., and E. R. Kinkead. 1973. Chronic inhalation toxicity of hydrazine. Proc, 4th Annual Conference of Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-73-125,* p 351-365.
13. Hawks, A., R. M. Hicks, J. W. Holsman, and P. N. Magee. 1974. Morphological and biochemical effects of 1,2-dimethylhydrazine and 1-methylhydrazine in rats and mice. *Brit. J. Cancer* 30:429.
14. Heck, W. W., M. E. Bloodworth, W. J. Clark, D. R. Darling, and W. Hoover. 1962. Environmental pollution by missile propellants. Wright-Patterson AFB, Oh. *AMRL-TDR-62-38.*
15. Heck, W. W., M. E. Bloodworth, W. J. Clark, D. R. Darling, and W. Hoover. 1963. Environmental pollution by missile propellants. Wright-Patterson AFB, Oh. *AMRL-TDR-63-75.*
16. Heinemann, J. M., and V. E. Rose. 1966. Aerozine-50 marine bioassays. Kelly AFB, Tx. *REHL No. 66-1.*
17. Hoover, W. L., M. E. Bloodworth, W. J. Clark, W. W. Heck, and L. Hold. 1964. Environmental pollution by missile propellants. Wright-Patterson AFB, Oh. *AMRL-TDR-64-5.*
18. Kato, R., A. Rakanaka, and H. Shoji. 1969. Inhibition of drug metabolizing enzymes of liver microsomes by hydrazine derivatives in relation to their lipid solubility. *Japanese J. Pharmacol.* 19:315-322.
19. Lurker, P. 1976. Catalytic deoxygenation of aqueous solution by hydrazine. Wright-Patterson AFB, Oh. *AMRL-TR-76-23.*
20. MacEwen, J. D., E. E. McConnell, and K. C. Back. 1974. The effects of 6-month chronic low level inhalation exposures to hydrazine on animals. Proc, 5th Annual Conference on Environmental Toxicology. Wright-Patterson AFB, Oh. *AMRL-TR-74-125,* p 225-237.
21. MacEwen, J. D., and E. H. Vernot. 1975. Toxic Hazards Research Unit annual technical report: 1975. Wright-Patterson AFB, Oh. *AMRL-TR-75-57,* pp. 43-55.
22. MacEwen, J. D., and E. H. Vernot. 1975. Toxic Hazards Research Unit annual technical report: 1975. Wright-Patterson AFB, Oh. *AMRL-TR-75-57,* pp. 101-111.
23. MacEwen, J. D., and E. H. Vernot. 1977. Toxic Hazards Research Unit annual technical report: 1977. Wright-Patterson AFB, Oh. *AMRL-TR-77-46,* pp. 16-19.
24. National Academy of Sciences-National Research Council, Committee on Toxicology. 1974. Guides for Short Term Exposures of the Public to Air Pollutants. V. Guide for Hydrazine, Monomethylhydrazine, and 1,1-Dimethylhydrazine. Available from National Technical Information

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Mortality of Aerospace Workers Exposed to Trichloroethylene

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We measured mortality rates in a cohort of 20,508 aerospace workers who were followed up over the period 1950–1993. A total of 4,733 workers had occupational exposure to trichloroethylene. In addition, trichloroethylene was present in some of the washing and drinking water used at the work site. We developed a job-exposure matrix to classify all jobs by trichloroethylene exposure levels into four categories ranging from "none" to "high" exposure. We calculated standardized mortality ratios for the entire cohort and the trichloroethylene-exposed subcohort. In the standardized mortality ratio analyses, we observed a consistent elevation for nonmalignant respiratory disease, which we attribute primarily to the higher background rates of respiratory disease in this region. We also compared trichloroethylene-exposed workers with workers in the "low" and "none" exposure categories. Mortality rate ratios for nonmalignant respiratory disease were near or less than 1.00 for trichloroethylene exposure groups. We observed elevated rate ratios for ovarian cancer among those with peak exposure at medium and high levels [relative risk (RR) = 2.74; 95% confidence interval (CI) = 0.84–8.99] and among women with high cumulative exposure (RR = 7.09; 95% CI = 2.14–23.54). Among those with peak exposures at medium and high levels, we observed slightly elevated rate ratios for cancers of the kidney (RR = 1.89; 95% CI = 0.85–4.23), bladder (RR = 1.41; 95% CI = 0.52–3.81), and prostate (RR = 1.47; 95% CI = 0.85–2.55). Our findings do not indicate an association between trichloroethylene exposure and respiratory cancer, liver cancer, leukemia or lymphoma, or all cancers combined. (Epidemiology 1998;9:424–431)

Keywords: aerospace workers, cancer, cohort study, healthy worker effect, respiratory disease, trichloroethylene.

Trichloroethylene (TCE) has been used in degreasing metal, processing food, and as an anesthetic agent. In 1992, the U.S. Environmental Protection Agency (EPA) withdrew its classification of TCE as a "probable human carcinogen."[1] In 1995, the International Agency for Research on Cancer (IARC) reclassified TCE to Category 2A, indicating that ". . . a positive association has been observed between exposure to the agent. . . and cancer. . . but chance, bias, or confounding could not be ruled out with reasonable confidence."[2] At least two reviewers questioned the IARC classification.[2,3]

Previous studies examined cohorts exposed either to TCE or to solvent mixtures containing TCE.[3–18] Of 15 published occupational mortality studies mentioning TCE, a few report positive associations, but among them, there is no consistent major increase in cancer mortality.[4–18] Weiss[3] recently reviewed studies of TCE production workers (Finland[19] and Sweden[4]), civilian air force employees (Utah[17]), and aerospace workers (Arizona; ENSR Health Sciences. Final Report: Historical Prospective Mortality Study of Hughes Aircraft Employees at Air Force Plant #44. ENSR Health Sciences, May 1990, unpublished report). He concluded that there was no excess cancer risk, with the possible exception of non-Hodgkin's lymphoma and cancers of the liver, biliary tract, and kidney.

Anttila *et al*[19] reported excess incidence of cancers of the stomach, liver, prostate, and lymphohematopoietic systems in Finnish workers exposed to organic solvents, including TCE. Henschler *et al*[20] reported excess incidence of renal cell cancers in a small (N = 169) heavily exposed cohort of German cardboard workers. In a study of aircraft maintenance workers, Spirtas *et al*[17] reported elevated standardized mortality ratios (SMRs) for biliary cancer among male employees and multiple myeloma and non-Hodgkin's lymphoma among female employees. Low SMRs were reported for all causes, all cancers combined, and nonmalignant respiratory diseases. Axelson *et al*[4] reported an excess of skin cancer among male Swedish workers identified through a TCE surveillance program. They also report standardized incidence ratios for men of 1.6 and 1.4 for non-Hodgkin's lymphoma and liver/biliary cancer, respectively. An earlier analysis of Hughes aircraft workers found no excess cancer risk or overall impact on mortality (ENSR Health Sciences, unpublished report).

Our study evaluates the mortality of the same cohort of employees working at a Hughes Aircraft manufactur-

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ing site in Arizona. Most TCE exposure occurred in vapor degreasing units between 1952 and 1977. Before 1981, the plant had used some contaminated well water (TCE levels estimated between 730 and 2,200 parts per billion) for showers and drinking. Thus, workers were potentially exposed through both occupation (inhalation and skin exposure) and water. We have now followed the cohort through 1993, with more extended analyses than the 1990 study of this cohort (ENSR Health Sciences, unpublished report).

Methods

From company records, we identified all workers who were employed at the plant for at least 6 months between January 1, 1950, and December 31, 1985. We determined vital status through the Social Security Administration (SSA) and National Death Index (NDI). We excluded 27 persons from the cohort because of missing information, leaving a cohort of 20,508 workers. Personnel data included name, Social Security number, date of birth, sex, race, date of hire, job title, and termination date. After ascertaining deaths through either SSA or NDI, we obtained death certificates from each state and coded cause of death according to the *International Classification of Diseases* (ICD) in use at time of death (revisions 7–9).

Because limited industrial hygiene measurements were available for the Hughes plant before 1975, Hughes employees with at least 30 years of experience rated TCE exposure for each job classification. Hughes industrial hygienists then compiled these ratings into a master exposure matrix that was reviewed and confirmed by the Hughes employees.

From the ratings, jobs were classified into exposure categories of high, medium, low, or none. The highest rating involved work on degreaser machines using TCE, which the industrial hygienists estimate were equivalent to exposures above 50 parts per million. Jobs with a medium rating were near the degreasing area, with more than occasional contact with TCE. A low exposure rating was given to jobs away from the degreasing area, but entailing occasional contact with TCE. All other jobs were assigned zero exposure. Most TCE-exposed workers had more than one category of exposure. We did not consider potential exposure to drinking or wash water in classifying occupational TCE exposure.

We assigned exposure scores of 0 for none, 1 for low, 4 for medium, and 9 for high exposure, which assumes a potential exponential exposure-response relation. We assigned a zero level to anyone with less than 6 months of any TCE exposure (N = 1,025). Then, for each job, we multiplied months of exposure by the TCE rating (0, 1, 4, or 9) and summed the results to arrive at a cumulative (total) exposure score. For internal cohort analyses, we created exposure groups using both cumulative exposure and the job with the highest TCE exposure rating ("peak" exposure). (We used "peak" exposure to evaluate hypotheses that high-level exposure involves different metabolic pathways and may, thus, be more important in assessing cancer risk.) In the SMR analyses, we used cumulative exposure scores and a dichotomous measure (none/any) to define exposure groups.

Statistical Analyses

We used the OCMAP-PC computer program to calculate SMRs and 95% confidence limits for the overall cohort and TCE-exposed subcohorts.[21] For internal cohort analyses, we used Mantel-Haenszel procedures and Cox proportional hazard models that included exposure classification, age at hire, and gender.[22] Data concerning race were too sparse to use in the stratified analyses or Cox models. Because we found that decade of hire did not influence relative risk estimates, we did not include it in the final Cox models. We analyzed all causes of death, nonmalignant respiratory disease, and selected cancer outcomes using three exposure classification systems (ever/never, peak, and cumulative).

To analyze peak exposure, we combined jobs with no and low exposure into one group and jobs with medium and high exposure into a second group. To define cumulative exposure categories, we examined the distribution of cumulative exposure scores to identify any obvious cutpoints. The distribution was approximately lognormal, with no obvious modes. Therefore, we divided the TCE-exposed group into "low" and "high" based on cumulative exposure score. Exposure groups were roughly equal (50%), with the low group including any workers with the equivalent of up to 5 years of exposure to jobs at low exposure or 1.4 years of medium exposure. The high-exposure group includes all other TCE-exposed workers.

Our SMR analyses include most causes of death. For internal cohort analyses, we selected outcomes either on the basis of previous reports or because of elevated SMRs in our analyses. Because results from the Mantel-Haenszel and Cox proportional hazards models were so similar, we present only Cox modeling results. Although we used the ever/never exposure classification in both SMR and internal cohort analyses, we do not report those results, because they are highly correlated with both peak and cumulative exposure classifications. (A full set of analytical tables is available upon request.)

For cancer sites previously identified as possibly TCE associated, we combined our data with previously published cohorts to calculate a series of meta-SMRs and associated confidence limits. We derived the meta-SMRs from the sums of observed and expected deaths.

Results

The cohort is composed primarily of white men, nearly half of whom were hired before 1960. Of 4,052 deaths, we were unable to locate 112 death certificates. Some occupational TCE exposure was experienced by 23% of the cohort (Table 1).

SMR Analysis

For the full cohort, most SMRs were below 1.00 (Table 2), with elevations for Hodgkin's disease (1.25) and

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TABLE 1. Distribution of Aerospace Worker Cohort by Sex, Race, Birth Decade, Hire Decade, and Exposure Classification

Demographic Factor	Nonexposed				TCE Exposed				Totals			
	N	%	PY*	%PY	N	%	PY	%PY	N	%	PY	%PY
Sex												
Male	11,187.0	70.9	250,410.0	70.4	2,555.0	54.0	57,879.0	54.7	13,742.0	67.0	308,289.0	66.8
Female	4,588.0	29.1	105,355.0	29.6	2,178.0	46.0	47,973.0	45.3	6,766.0	33.0	153,328.0	33.2
									20,508.0		461,617.0	
Race												
White	14,698.0	93.2	331,072.0	93.1	4,132.0	87.3	91,561.0	86.5	18,830.0	91.8	422,633.0	91.6
Nonwhite	1,077.0	6.8	24,693.0	6.9	601.0	12.7	14,291.0	13.5	1,678.0	8.2	38,984.0	8.4
									20,508.0		461,617.0	
Birth year												
1920	3,168.0	20.1	88,953.0	25.0	1,022.0	21.6	29,711.0	28.1	4,190.0	20.4	118,664.0	25.7
1920–1929	3,171.0	20.1	96,152.0	27.0	893.0	18.9	23,950.0	22.6	4,064.0	19.8	120,102.0	26.0
1930–1939	3,252.0	20.6	89,186.0	25.1	803.0	17.0	19,382.0	18.3	4,055.0	19.8	108,568.0	23.5
1940–1949	2,288.0	14.5	37,968.0	10.7	1,008.0	21.3	19,779.0	18.7	3,296.0	16.1	57,747.0	12.5
1950–1959	2,840.0	18.0	33,669.0	9.5	749.0	15.8	10,558.0	10.0	3,589.0	17.5	44,227.0	9.6
≤1960	1,056.0	6.7	9,838.0	2.8	258.0	5.5	2,472.0	2.3	1,314.0	6.4	12,310.0	2.7
									20,508.0		461,618.0	
Hire date												
<1960†	6,941.0	44.0	222,557.0	62.6	1,563.0	33.0	48,779.0	46.1	8,504.0	41.5	271,336.0	58.8
1960–1969	1,782.0	11.3	44,080.0	12.4	913.0	28.8	23,045.0	21.8	2,695.0	13.1	67,125.0	14.5
1970–1979	2,448.0	15.5	42,545.0	12.0	1,322.0	18.9	24,625.0	23.3	3,770.0	18.4	67,170.0	14.6
1980–1989	4,604.0	29.2	46,584.0	13.1	935.0	16.5	9,403.0	8.9	5,539.0	27.0	55,987.0	12.1
Totals	15,775.0	76.9	355,766.0	77.1	4,733.0	23.1	105,852.0	18.7	20,508.0	100	461,618.0	100.0

* PY = person-years.
† Only 27 employees started before 1950.

kidney cancer (1.14), although confidence intervals (CI) were wide (95% CI = 0.60–2.30 and 0.78–1.61, respectively). SMRs for all respiratory diseases and for suicide were also elevated. For these conditions, Arizona rates are considerably higher than national rates. When we used Arizona rates for comparison instead of U.S. rates, SMRs were lower (data not shown).

The TCE-exposed subcohort results resembled the total cohort SMRs for most causes of death (Table 2). SMRs for respiratory disease (1.14; 95% CI = 0.92–1.41) and kidney cancer (1.32; 95% CI = 0.57–2.60) were elevated, but with wide confidence intervals. SMRs for prostate (1.18; 95% CI = 0.73–1.80), respiratory (1.12; 95% CI = 0.91–1.35), bladder (1.36; 95% CI = 0.59–2.68), and ovarian (1.21; 95% CI = 0.52–2.38) cancers, which were all below 1.00 in the overall cohort analysis, were slightly elevated in the TCE-exposed subcohort analysis, although, again, with wide confidence intervals. For respiratory cancers, we observed higher SMRs in the low-exposure category than in the high-exposure group. We also examined SMRs among the nonexposed subcohort (data not shown). These results were similar to the SMRs for the overall cohort.

Internal Cohort Analysis

Our Cox proportional hazards modeling results are presented in Tables 3–5. For all cancers and nonmalignant respiratory disease, all risk ratios for peak and cumulative exposure classifications were near 1.00 (Table 3). The risk ratio for respiratory cancers in the low-cumulative-exposure group was 1.47 (95% CI = 1.07–2.03); however, both peak- and high-cumulative-exposure groups had risk ratios near 1.00 (Table 3).

For cancers of the lymphatic and hematopoietic systems (Table 4), risk ratios were close to 1.00 for all of these cancers combined and for leukemia. For lymphosarcoma and reticulosarcoma, the risk ratios were slightly elevated for the peak-exposure and the low-cumulative-exposure groups; however, these estimates had wide confidence intervals. For the high-cumulative-exposure group, the risk ratio was 0.81, indicating lack of a dose-response effect. There were 11 cases of Hodgkin's disease in the cohort; because only one case was in the TCE-exposed group (Table 2), we did not conduct internal cohort analyses on this outcome.

For liver, kidney, bladder, prostate, and ovarian cancer, we observed somewhat higher associations with TCE exposure, but with varying confidence intervals (Table 5). These are based on only a few exposed cases, uniformly leading to wide confidence intervals. For bladder and ovarian cancers in the high-exposure categories, the confidence intervals were 1.10–6.65 and 2.14–23.54, respectively. For liver cancers, there was no association with the peak exposure classification, nor was there an apparent dose-response trend for cumulative exposure. Kidney cancers had a higher association (RR = 1.89; 95% CI = 0.85–4.23) with peak exposure than high cumulative exposure (RR = 1.59; 95% CI = 0.68–3.71). Ovarian cancers had the highest associations with TCE exposure for peak (RR = 2.74) and high cumulative exposures (RR = 7.09).

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TABLE 2. Standardized Mortality Ratios* for Selected Causes of Death: Overall Cohort and Occupationally Exposed Trichloroethylene Subcohort

Cause of Death†,‡	Overall Cohort (N = 20,508)				TCE-Exposed Subcohort (N = 4,733)			
	Observed	Expected	SMR	95% CI	Observed	Expected	SMR	95% CI
All causes of death	4,052	4,772.5	0.85	0.82–0.88	917	1,088.8	0.84	0.79–0.90
All malignant neoplasms	1,100	1,267.3	0.87	0.82–0.92	270	295.0	0.92	0.81–1.03
Cancer of digestive organs and peritoneum	255	307.8	0.83	0.73–0.94	55	71.3	0.77	0.58–1.00
Cancer of rectum	18	25.3	0.71	0.42–1.13	6	5.7	1.06	0.39–2.31
Cancer of biliary passages and liver	20	26.0	0.77	0.47–1.19	6	6.1	0.98	0.36–2.13
Cancer of pancreas	47	61.9	0.76	0.56–1.01	11	14.4	0.76	0.38–1.37
Cancer of respiratory system	401	424.0	0.95	0.86–1.04	103	92.4	1.12	0.91–1.35
Cancer of bronchus, trachea, lung	388	404.9	0.96	0.87–1.06	97	88.3	1.10	0.89–1.34
Cancer of breast	47	62.8	0.75	0.55–1.00	16	21.3	0.75	0.43–1.22
Cancer of uterus (women only)	6	17.4	0.34	0.13–0.75	1	6.1	0.16	0.00–0.91
Cancer of cervix uteri (women only)	1	10.0	0.10	0.00–0.56	0	3.5	0.00	0.00–1.07
Cancer of ovary (women only)	13	19.4	0.67	0.36–1.15	8	6.6	1.21	0.52–2.38
Cancer of prostate (men only)	76	81.4	0.93	0.74–1.17	21	17.8	1.18	0.73–1.80
Cancer of kidney	32	28.0	1.14	0.78–1.61	8	6.1	1.32	0.57–2.60
Cancer of bladder	23	27.3	0.84	0.53–1.26	8	5.9	1.36	0.59–2.68
Cancer of central nervous system	28	33.3	0.84	0.56–1.22	4	7.3	0.55	0.15–1.40
Cancer of all lymphatic, hematologic tissue	107	111.5	0.96	0.79–1.16	25	25.2	0.99	0.64–1.47
Lymphosarcoma and reticulosarcoma	11	14.2	0.78	0.39–1.39	3	3.1	0.96	0.20–2.81
Hodgkin's disease	10	8.0	1.25	0.60–2.30	1	1.7	0.60	0.02–3.35
Leukemia and aleukemia	42	42.8	0.98	0.71–1.33	10	9.5	1.05	0.50–1.93
Cancer of all other lymphopoietic tissue	44	46.5	0.95	0.69–1.27	11	10.9	1.01	0.51–1.81
All heart disease	1,409	1,751.5	0.80	0.76–0.85	290	387.5	0.75	0.67–0.84
Cerebrovascular disease	170	278.0	0.61	0.52–0.71	40	67.4	0.59	0.42–0.81
Nonmalignant respiratory disease	389	337.7	1.15	1.04–1.27	87	76.1	1.14	0.92–1.41
Bronchitis, emphysema, asthma	116	71.1	1.63	1.35–1.96	27	15.7	1.72	1.13–2.50
Emphysema	66	51.5	1.28	0.99–1.63	15	11.1	1.36	0.76–2.23
Other nonmalignant respiratory disease	171	153.9	1.11	0.95–1.29	39	34.8	1.12	0.80–1.53
Cirrhosis of liver	65	115.0	0.57	0.44–0.72	14	25.3	0.55	0.30–0.93
All external causes of death	293	366.7	0.80	0.71–0.90	68	80.1	0.85	0.66–1.08
Accidents	156	225.0	0.69	0.59–0.81	41	48.9	0.84	0.60–1.14
Suicides	115	89.1	1.29	1.07–1.55	20	18.4	1.09	0.67–1.68
Other causes of death	379	483.9	0.78	0.71–0.87	101	114.2	0.89	0.72–1.08

	Low (N = 2,357)				High (N = 2,376)			
	Observed	Expected	SMR	95% CI	Observed	Expected	SMR	95% CI
All causes of death	345	402.44	0.86	0.77–0.95	572	686.31	0.83	0.77–0.91
All malignant neoplasms	114	109.31	1.04	0.86–1.25	156	185.73	0.84	0.71–0.98
Cancer of digestive organs and peritoneum	21	25.92	0.81	0.50–1.24	34	45.41	0.75	0.52–1.05
Cancer of rectum	1	2.03	0.49	0.01–2.74	5	3.63	1.38	0.45–3.21
Cancer of biliary passages and liver	3	2.28	1.32	0.27–3.85	3	3.85	0.78	0.16–2.28
Cancer of pancreas	5	5.25	0.95	0.31–2.22	6	9.16	0.66	0.24–1.43
Cancer of respiratory system	46	31.59	1.46	1.07–1.94	57	60.81	0.94	0.71–1.21
Cancer of bronchus, trachea, lung	45	30.2	1.49	1.09–1.99	52	58.1	0.90	0.67–1.20
Cancer of breast	11	10.72	1.03	0.51–1.84	5	10.55	0.47	0.15–1.11
Cancer of uterus (women only)	1	3.28	0.31	0.01–1.70	0	2.84	0.00	0.00–1.30
Cancer of cervix uteri (women only)	0	1.91	0.00	0.00–1.93	0	1.54	0.00	0.00–2.39
Cancer of ovary (women only)	2	3.4	0.61	0.07–2.21	6	3.4	1.79	0.66–3.88
Cancer of prostate (men only)	7	5.42	1.29	0.52–2.66	14	12.41	1.13	0.62–1.89
Cancer of kidney	1	2.13	0.47	0.01–2.62	7	3.94	1.78	0.72–3.66
Cancer of bladder	1	1.97	0.51	0.01–2.83	7	3.90	1.79	0.72–3.69
Cancer of central nervous system	2	2.7	0.73	0.09–2.64	2	4.6	0.44	0.05–1.58
Cancer of all lymphatic, hematologic tissue	10	9.37	1.07	0.51–1.96	15	15.81	0.95	0.53–1.57
Lymphosarcoma and reticulosarcoma	2	1.12	1.79	0.22–6.46	1	2.00	0.50	0.01–2.79
Hodgkin's disease	1	0.65	1.55	0.04–8.64	0	1.02	0.00	0.00–3.61
Leukemia and aleukemia	3	3.55	0.85	0.17–2.47	7	5.98	1.17	0.47–2.41
Cancer of all other lymphopoietic tissue	4	4.05	0.99	0.27–2.53	7	6.80	1.03	0.41–2.12
All heart disease	77	136.78	0.56	0.44–0.70	213	250.72	0.85	0.74–0.97
Cerebrovascular disease	17	25.71	0.66	0.39–1.06	23	41.73	0.55	0.35–0.83
Nonmalignant respiratory disease	32	27.00	1.19	0.81–1.67	55	49.06	1.12	0.84–1.46
Bronchitis, emphysema, asthma	11	5.42	2.03	1.01–3.63	16	10.27	1.56	0.89–2.53
Emphysema	5	3.66	1.37	0.44–3.19	10	7.42	1.35	0.65–2.48
Other nonmalignant respiratory disease	13	12.11	1.07	0.57–1.84	26	22.66	1.15	0.75–1.68
Cirrhosis of liver	9	9.49	0.95	0.43–1.80	5	15.85	0.32	0.10–0.74
All external causes of death	27	32.77	0.82	0.54–1.20	41	47.36	0.87	0.62–1.18
Accidents	18	19.68	0.92	0.54–1.45	23	29.18	0.79	0.50–1.18
Suicides	6	7.23	0.83	0.31–1.81	14	11.14	1.26	0.69–2.11
Other causes of death	46	44.00	1.05	0.77–1.39	55	70.16	0.78	0.59–1.02

*U.S. mortality rates, 1950–1992, provided by OCMAP software (see Ref 21). SMR = standardized mortality ratio.
†Totals do not add up to "All causes" total deaths because not all specific causes are presented.
‡"Other causes" does not include all other cause ICD codes (see Appendix).

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TABLE 3. All Cancers and Respiratory Diseases: Internal Cohort Analyses for Peak and Cumulative Trichloroethylene Exposure Classifications Using Cox Proportional Hazards Models

	Exposed (N)	Unexposed (N)	RR*	95% CI
All cancers				
Peak: medium and high *vs* low and no exposure	177	923	1.06	0.90–1.24
Cumulative (low)	114	830	1.22	0.99–1.49
Cumulative (high)	156	830	1.01	0.85–1.19
Nonmalignant respiratory disease				
Peak: medium and high *vs* low and no exposure	59	330	0.97	0.73–1.28
Cumulative (low)	32	302	1.01	0.70–1.47
Cumulative (high)	55	302	0.99	0.75–1.33
Cancer of bronchus, trachea, lung				
Peak: medium and high *vs* low and no exposure	64	324	1.07	0.82–1.40
Cumulative (low)	45	291	1.47	1.07–2.03
Cumulative (high)	52	291	0.96	0.72–1.29

* RR = relative risk.

The meta-SMRs, which combine results from the four TCE cohorts cited by Weiss,[3] were all near 1.00, ranging from 1.09 for prostate and kidney cancers to 1.25 and 1.32 for non-Hodgkin's lymphoma and liver cancer, respectively (Table 6).

Discussion

Our data offer little support for an association between TCE exposure and cancer mortality from leukemia, cancer in hematopoietic tissues, and digestive, liver, and respiratory cancers. Our findings for kidney, bladder, prostate, and ovarian cancers are limited by small numbers, lack of information on smoking, and lack of quantitative exposure information.

Our finding of a potential association between TCE and ovarian cancer has not been previously reported. Among the TCE studies, Anttila *et al*[19] found no excess risk, and Spirtas *et al*[17] reported similar findings (SMR = 1.01). A hospital-based case-control study in the Washington DC area found no important association between ovarian cancer and occupational solvent or polycyclic aromatic hydrocarbon exposures; however, only a few participants in this study held manufacturing jobs.[23] We observed 13 such cancers in the entire cohort and 8 among the TCE-exposed subcohort. The expected numbers in the SMR analyses were 19.4 and 6.6, respectively. That six of the eight exposed cases were classified as "high" TCE exposure accounts for the high rate ratios.

Risk factors for ovarian cancer include family history of ovarian cancer, use of infertility drugs, and a long history of unprotected intercourse.[24] Protective factors for ovarian cancer include use of oral contraceptives, number of pregnancies, breastfeeding, and history of gynecologic surgery.[23,24] We reviewed the death certificates for these deaths and did not find any similarity in last names that could suggest a potential cluster of ovarian cancer cases among the same families. This review is limited because we relied only on names of workers in the cohort; we did not conduct interviews or collect other data on family history of ovarian cancer. Our results are dependent on six exposed cases, and exposure misclassification or another cause from a competing risk factor in one or two cases could substantially reduce the association. The lack of previous research suggesting ovarian cancer risk, the small number of cases involved, the largely unknown etiology of ovarian cancer, and the numerous unmeasured potential confounding factors limit our ability to interpret these findings.

TABLE 4. Lymphatic and Hematopoietic Cancers: Internal Cohort Analyses for Peak and Cumulative Trichloroethylene Exposure Using Cox Proportional Hazards Models

	Exposed (N)	Unexposed (N)	RR*	95% CI
Lymphatic and hematopoietic cancers				
Peak: medium and high *vs* low and no exposure	17	90	1.08	0.64–1.82
Cumulative (low)	10	82	1.09	0.56–2.14
Cumulative (high)	15	82	1.03	0.59–1.79
Leukemia				
Peak: medium and high *vs* low and no exposure	7	35	1.10	0.49–2.49
Cumulative (low)	3	32	0.69	0.21–2.32
Cumulative (high)	7	32	1.14	0.50–2.60
Lymphosarcoma and reticulosarcoma				
Peak: medium and high *vs* low and no exposure	2	9	1.31	0.28–6.08
Cumulative (low)	2	8	2.25	0.46–11.09
Cumulative (high)	1	8	0.81	0.10–6.49

* RR = relative risk.

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TABLE 5. Liver, Kidney, Bladder, Prostate, and Ovarian Cancers: Internal Cohort Analyses for Peak and Cumulative Trichloroethylene Exposure Using Cox Proportional Hazards Models

	Exposed (N)	Unexposed (N)	RR*	95% CI
Liver cancer†				
Peak: medium and high *vs* low and no exposure	3	17	0.98	0.29–3.35
Cumulative (low)	3	14	2.12	0.59–7.66
Cumulative (high)	3	14	1.19	0.34–4.16
Kidney cancer†				
Peak: medium and high *vs* low and no exposure	8	24	1.89	0.85–4.23
Cumulative (low)	1	24	0.31	0.04–2.36
Cumulative (high)	7	24	1.59	0.68–3.71
Bladder cancer‡				
Peak: medium and high *vs* low and no exposure	5	18	1.41	0.52–3.81
Cumulative (low)	1	15	0.69	0.09–5.36
Cumulative (high)	7	15	2.71	1.10–6.65
Prostate cancer‡				
Peak: medium and high *vs* low and no exposure	16	60	1.47	0.85–2.55
Cumulative (low)	7	55	1.05	0.48–2.32
Cumulative (high)	14	55	1.35	0.75–2.44
Ovarian cancer‡				
Peak: medium and high *vs* low and no exposure	4	9	2.74	0.84–8.99
Cumulative (low)	2	5	3.45	0.66–17.97
Cumulative (high)	6	5	7.09	2.14–23.54

* RR = relative risk.
† Cox models include age and sex as independent variables.
‡ Cox models include age only as independent variable.

To compare these updated results with previous research, we calculated meta-SMRs for liver, prostate, and kidney cancers and non-Hodgkin's lymphoma across the studies evaluated in the recent review by Weiss.[3] Although these four studies do not represent the complete set of TCE studies, IARC considered three of them to be the most relevant for assessing TCE carcinogenicity.[4,17,19] In general, the meta-SMRs offer little support for a relation between TCE exposure and non-Hodgkin's lymphoma or cancers of the kidney, bladder, and prostate (Table 6). Small numbers of cases (except for prostate cancer), even aggregated across all four studies, further limit causal interpretation of these findings.

To address the pronounced healthy worker effect (HWE) in this cohort, we used Cox proportional hazards models, using peak and cumulative exposures. In our study, however, the Cox method is limited by small numbers of cancers in the exposed, unexposed, or both

TABLE 6. Meta-Analysis of Four Occupational Cohort Mortality Studies with Exposure to Trichloroethylene

Cancer Site	Finnish*	Swedish†	Civilian Air Force‡	Aerospace Workers§	Total	Meta-SMR‖	95% CI
Liver							
Observed	5	4	2	6	17	1.32	0.77–2.11
Expected	2.2	2.8	1.8	6.1	12.9		
Prostate							
Observed	13	26	22	21	82	1.09	0.87–1.36
Expected	9.4	20.7	27.6	17.8	75.5		
Kidney							
Observed	6	6	8	8	28	1.09	0.72–1.58
Expected	6.9	5.2	7.5	6.1	25.7		
Bladder							
Observed	5	8	11	8	32	1.15	0.78–1.62
Expected	6.1	7.9	7.9	5.9	27.8		
Non-Hodgkin's lymphoma							
Observed	8	5	14	14	41	1.25	0.89–1.70
Expected	4.4	3.2	11.2	14	32.8		

* Anttila *et al*, 1995.[19]
† Axelson *et al*, 1994.[4]
‡ Spirtas *et al*, 1991.[17]
§ Present study.
‖ SMR = standardized mortality ratio.

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groups. Thus, narrowly defining exposure groups, although reducing potential exposure misclassification, creates smaller groups and thereby produces more imprecise estimates of relative risk. These factors have to be considered in interpreting the results of our internal comparisons. The small number of cases in the TCE subcohort limits our ability to assess the risks for rare cancers. In addition, although nearly two-thirds of the TCE-exposed cohort were followed for more than 20 years (Table 1), it is possible that higher risks could occur later.

In addition to its limited data, this study has other limitations. We lack data on potential confounders such as smoking, diet, or exposure to other solvents. Furthermore, with no direct measurement of personal exposure, we had to rely on experts to assign estimated levels of TCE exposure, although we believe the extensive review process should have helped to reduce exposure misclassification.

The recent IARC review of TCE carcinogenicity considered positive findings from three occupational studies[4,17,19] for liver/biliary cancer and non-Hodgkin's lymphoma as suggestive of TCE carcinogenicity.[2] Our results and the meta-SMRs do not indicate strong effects on cancer risk for these outcomes.

References

1. IRIS (Integrated Risk Information System). Trichloroethylene. [Data online] Washington DC: Environmental Protection Agency, 1992. Available from National Library of Medicine, Bethesda, MD.
2. International Agency for Research on Cancer. Monographs on the Evaluation of the Carcinogenic Risks to Humans; Dry Cleaning, Some Chlorinated Solvents and Other Industrial Chemicals. vol. 63. Lyon: International Agency for Research on Cancer, 1995.
3. Weiss NS. Cancer in relation to occupational exposure to trichloroethylene. Occup Environ Med 1996;53:1–5.
4. Axelson O, Selden A, Andersson K, Hogstedt C. Updated and expanded Swedish cohort study on trichloroethylene and cancer risk. J Occup Med 1994;36:556–562.
5. Barret L, Faure J, Daniel V. Epidemiologic study of cancer in a community of workers occupationally exposed to trichloroethylene and cutting oils (Abstract). J Clin Toxicol 1985;23:438.
6. Blair A. Mortality among workers in the metal polishing and plating industry, 1951–1969. J Occup Med 1980;22:158–162.
7. Fredriksson M, Bengtsson NO, Hardell L, Axelson O. Colon cancer, physical activity, and occupational exposures: a case-control study. Cancer 1989; 63:1838–1842.
8. Garabrant D, Held J, Langholz B, Bernstein L. Mortality of aircraft manufacturing workers in southern California. Am J Ind Med 1988;13:683–693.
9. Greenland S, Salvan A, Wegman D, Hallock M, Smith T. A case-control study of cancer mortality at a transformer-assembly facility. Int Arch Occup Environ Health 1994;66:49–54.
10. Hardell L, Eriksson M, Lenner P, Lundgren E. Malignant lymphoma and exposure to chemicals especially organic solvents, chlorophenols and phenoxy acids: a case-control study. Br J Cancer 1981;43:169–176.
11. Heineman E, Cocco P, Gómez M, Dosemeci M, Stewart PA, Hayes RB, Zahm SH, Thomas TL, Blair A. Occupational exposure to chlorinated aliphatic hydrocarbons and risk of astrocytic brain cancer. Am J Ind Med 1994;26:155–169.
12. Lowengart RA, Peters JM, Cicioni C, Buckley J, Bernstein L, Preston-Martin S, Rappaport E. Childhood leukemia and parents' occupational and home exposures. J Natl Cancer Inst 1987;79:39–46.
13. Novotna E, David A, Malek B. An epidemiological study on hepatic tumor incidence in subjects working with trichloroethylene. I. Negative result of retrospective investigations in subjects with primary liver carcinoma (Abstract). Prac Lek 1979;31:121–123.
14. Paddle GM. Incidence of liver cancer and trichloroethylene manufacture: joint study by industry and a cancer registry. BMJ 1983;286:846.
15. Shannon HS, Haines T, Bernholz C, Julian JA, Verma DK, Jamieson E, Walsh C. Cancer morbidity in lamp manufacturing workers. Am J Ind Med 1988;14:281–290.
16. Shindell S, Ulrich S. A cohort study of employees of a manufacturing plant using trichloroethylene. J Occup Med 1985;27:577–579.
17. Spirtas R, Stewart PA, Lee JS, Marano DE, Forbes CD, Grauman DJ, Pettigrew HM, Blair A, Hoover RN, Cohen JL. Retrospective cohort mortality study of workers at an aircraft maintenance facility. I. Epidemiological results. Br J Ind Med 1991;48:515–530.
18. Tola S, Vilhunen R, Jarvinen E, Korkala M. A cohort study on workers exposed to trichloroethylene. J Occup Med 1980;22:737–740.
19. Anttila A, Pukkala E, Sallmen M, Hernberg S, Hemminki K. Cancer incidence among Finnish workers exposed to halogenated hydrocarbons. J Occup Environ Med 1995;37:797–806.
20. Henschler D, Vamvakas S, Lammert M, Dekant W, Kraus B, Thomas B, Ulm K. Increased incidence of renal cell tumors in a cohort of cardboard workers exposed to trichloroethene. Arch Toxicol 1995;69:291–299.
21. Marsh GM, Preininger M. OCMAP: a user-oriented occupational cohort mortality analysis program. Am Stat 1980;34:245–246.
22. Cox DR. Regression models and life tables. J R Stat Soc Ser B 1972;34: 187–202.
23. Hartge P, Stewart P. Occupation and ovarian cancer: a case-control study in the Washington, DC, metropolitan area, 1978–1981. J Occup Med 1994; 36:924–927.
24. Whittemore AS, Harris R, Itnyre J, and the Collaborative Ovarian Cancer Group. Characteristics relating to ovarian cancer risk: collaborative analysis of 12 US case-control studies. II Invasive epithelial ovarian cancers in white women. Am J Epidemiol 1992;36:1184–1203.

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HYDRAZINE

302-01-2

Hazard Summary

- Symptoms of acute (short-term) exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and central nervous system in humans. The liquid is corrosive and may produce **chemical burns and severe dermatitis** from skin contact.
- Information is not available on the chronic (long-term) effects of hydrazine in humans. In rats chronically exposed to hydrazine by inhalation, inflammatory changes of the respiratory tract were observed. In another chronic inhalation study, rats demonstrated depressed growth rates, liver damage occurred in mice, and fatty changes in the liver and spleen were reported in dogs.
- The U.S. Environmental Protection Agency (EPA) has not established a Reference Concentration (RfC) or a Reference Dose (RfD) for hydrazine.
- Information is not available on the reproductive or developmental effects of hydrazine in humans. Hydrazine is **fetotoxic to rodents** exposed by injection. Reduced ratio of fetal survivors to implantation sites, reduced fetal weight, and generalized edema, but no gross malformations were observed in rats.
- Adequate information is not available on the carcinogenic effects of hydrazine in humans. Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. EPA has classified hydrazine as a Group B2, **probable human carcinogen of high carcinogenic hazard**, with a $1/ED_{10}$ value of 107 per $(mg/kg)d^a$ and an inhalation unit risk estimate of 4.9×10^{-3} $(g/m^3)^{-1}$.

[a] The $1/ED_{10}$ value is a measure of the carcinogenic potency of a chemical. The value reported here has been proposed in the hazard ranking of hazardous air pollutants in EPA's proposed rulemaking (Section 112(g) of the Clean Air Act, April 1994).

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of hydrazine including the unit cancer risk for inhalation exposure, and EPA's *Health and Environmental Effects Profile for Hydrazine*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Individuals may be occupationally exposed to hydrazine in the workplace. (1,2)
- Accidental discharge into water, air, and soil may occur during storage, handling, transport, and improper waste disposal. However, hydrazine rapidly degrades in the environment and is rarely encountered. (2,3)
  Hydrazine has been detected in tobacco smoke. (2)

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- Hydrazine has been detected in tobacco smoke. (2)

Assessing Personal Exposure

- Hydrazine may be detected in the blood of exposed individuals. (1,2)

Health Hazard Information

Acute Effects:

- Symptoms of acute (short-term) exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and CNS in humans. (2-4)
- The liquid is corrosive and may produce chemical burns and severe dermatitis from skin contact. (1,4)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated hydrazine to have high acute toxicity from inhalation and ingestion and extreme acute toxicity from dermal exposure. (5)

Chronic Effects (Noncancer):

- Information is not available on the chronic (long-term) effects of hydrazine in humans.
- In rats chronically exposed to hydrazine by inhalation, inflammatory changes of the respiratory tract were observed. In another chronic inhalation study, rats demonstrated depressed growth rates, liver damage occurred in mice, and fatty changes in the liver and spleen were reported in dogs. (6)
- EPA has not established an RfC or an RfD for hydrazine. (4)

Reproductive/Developmental Effects:

- Information is not available on the reproductive or developmental effects of hydrazine in humans.
- Hydrazine is fetotoxic to rodents exposed by injection. Reduced ratio of fetal survivors to implantation sites, reduced fetal weight, and no gross malformations, but generalized edema, were observed in rats. (6)

Cancer Risk:

- Adequate information is not available on the carcinogenic effects of hydrazine in humans.
- Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. (4,6,7)
- EPA has classified hydrazine as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.9×10^{-3} $(g/m^3)^{-1}$. EPA estimates that, if an individual were to breathe air containing hydrazine at 0.0002 g/m^3(1) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.002 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.02 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. (4)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has ranked hydrazine in the nonthreshold category. The 1/ED

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the Clean Air Act Amendments, has ranked hydrazine in the nonthreshold category. The $1/ED_{10}$ value is 107 per (mg/kg)/d and this would place it in the high category under Superfund's ranking for carcinogenic hazard. ( )

Physical Properties

- The chemical formula for hydrazine is H_4N_2, and its molecular weight is 32.05 g/mol. (6)
- Hydrazine occurs as a colorless, oily, flammable liquid that is miscible with water. (6,8)
- Hydrazine has a penetrating odor, resembling that of ammonia, with an odor threshold of 3.7 ppm. (8,9)
- The vapor pressure for hydrazine is 14.4 mm Hg at 25 C, and its log octanol/water partition coefficient (log K_{ow}) is 0.08. (6)

Uses

- Hydrazine is used in agricultural chemicals (pesticides), blowing agents, pharmaceutical intermediates, photography chemicals, water treatment for corrosion protection, textile dyes, and jet and rocket fuel. (4,6,8)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For hydrazine: 1 ppm = 1.31 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000.0			
-- -- -- -- 100.0	• LC_{50} (rats) (747 mg/m^3) • LC_{50} (mice) (330 mg/m^3)		5 5
-- -- -- -- 10.0			
-- -- -- -- 1.0		• MSHA standard (1.3 mg/m^3)	5
-- -- -- -- 0.1		• OHSA PEL (0.1 mg/m^3)	5

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-- -- -- -- 0.01		• ACGIH TLV (0.01 mg/m^3)	5
-- -- -- -- 0.001			
-- -- -- -- 0.0001			
-- -- -- -- 0.00001			
-- -- -- -- 0.000001			
-- -- -- -- 0.0000001	• EPA Cancer Risk Level (1-in-a-million excess lifetime risk) = 2.0×10^{-7} mg/m^3		3

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
MSHA--Mine Safety and Health Administration.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
2. World Health Organization. *Environmental Health Criteria 68: Hydrazine*. Geneva, Switzerland. 1987.
3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda,

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MD. 1993.
4. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Hydrazine/Hydrazine Sulfate*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
6. U.S. Environmental Protection Agency. *Health and Environmental Effects Profile for Hydrazine and Hydrazine Sulfate*. EPA/600/x-84/332. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.
7. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents*. Volume 4. World Health Organization, Lyon. 1974.
8. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
9. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

1. *Micrograms per cubic meter is the unit of measurement for chemicals in air.

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United States Environmental Protection Agency

Integrated Risk Information System Logo

Hydrazine/Hydra
CASRN 302-
(03/01/9

Contents

I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

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VI. BIBLIOGRAPHY

VII. REVISION HISTORY

VIII. SYNONYMS

0352
Hydrazine/Hydrazine sulfate; CASRN 302-01-2 (03/01/97)

Health assessment information on a chemical substance is included in IRIS only after a comprehensive review of chronic toxicity data by U.S. EPA health scientists from several Program Offices and the Office of Research and Development. The summaries presented in Sections I and II represent a consensus reached in the review process. Background information and explanations of the methods used to derive the values given in IRIS are provided in the Background Documents.

STATUS OF DATA FOR Hydrazine/Hydrazine sulfate

File On-Line 09/07/88

Category (section)	Status	Last Revised
Oral RfD Assessment (I.A.)	no data	
Inhalation RfC Assessment (I.B.)	no data	
Carcinogenicity Assessment (II.)	on-line	04/01/91

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_I. CHRONIC HEALTH HAZARD ASSESSMENTS FOR NONCARCINOGENIC EFFECTS

__I.A. REFERENCE DOSE FOR CHRONIC ORAL EXPOSURE (RfD)

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2

Not available at this time.

__I.B. REFERENCE CONCENTRATION FOR CHRONIC INHALATION EXPOSURE (RfC

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2

Not available at this time.

_II. CARCINOGENICITY ASSESSMENT FOR LIFETIME EXPOSURE

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2
Last Revised -- 04/01/91

Section II provides information on three aspects of the carcinogenic assessment for the substance in question; the weight-of-evidence judgment of the likelihood that the substance is a human carcinogen, and quantitative estimates of risk from oral exposure and from inhalation exposure. The quantitative risk estimates are presented in three ways. The slope factor is the result of application of a low-dose extrapolation procedure and is presented as the risk per (mg/kg)/day. The unit risk is the quantitative estimate in terms of either risk per ug/L drinking water or risk per ug/cu.m air breathed. The third form in which risk is presented is a drinking water or air concentration providing cancer risks of 1 in 10,000, 1 in 100,000 or 1 in 1,000,000. The rationale and methods used to develop the carcinogenicity information in IRIS are described in The Risk Assessment Guidelines of 1986 (EPA/600/8-87/045) and in the IRIS Background Document. IRIS summaries developed since the publication of EPA's more recent Proposed Guidelines for Carcinogen Risk Assessment also utilize those Guidelines where indicated

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(Federal Register 61(79):17960-18011, April 23, 1996). Users are referred to Section I of this IRIS file for information on long-term toxic effects other than carcinogenicity.

II.A. EVIDENCE FOR CLASSIFICATION AS TO HUMAN CARCINOGENICITY

II.A.1. WEIGHT-OF-EVIDENCE CLASSIFICATION

Classification -- B2; probable human carcinogen.

Basis -- Tumors have been induced in mice, rats and hamsters following oral, inhalation or intraperitoneal administration of hydrazine and hydrazine sulfate. Hydrazine is mutagenic in numerous assays.

II.A.2. HUMAN CARCINOGENICITY DATA

Inadequate. A Letter to the Editor by Roe (1978) is the only available report on effects of hydrazine exposure in humans. Mortality data from two hydrazine manufacturing plants (from one company of nine in the field) are presented. Between 1963 and 1975, one company reported two deaths. Both were due to heart disease and were presumed to be unrelated to hydrazine exposure. A second company reported 26 deaths among 272 workers who had been employed at the plant between 1945 and 1970. Two of these deaths were due to stomach cancer. The author noted that the observed and expected deaths were similar and that these occupational exposures to hydrazine are not associated with an increased risk of cancer.

II.A.3. ANIMAL CARCINOGENICITY DATA

Sufficient. Biancifiori (1970) conducted a multiple-dose study in which hydrazine sulfate was administered by gavage to groups of 24 to 30 8-week-old CBA/Cb/Se mice of each sex at doses of 0.0, 0.14, 0.28, 0.56, or 1.13 mg/day, 6 days/week for 25 weeks. Animals were observed throughout their lifetimes. Liver carcinomas were induced in a dose-related manner in both sexes and lung metastases were observed in some of the mice treated with 1.13 mg/kg/day. Pulmonary tumors were reportedly present in many of the treated mice, but incidences were not reported because the purpose of the study was to describe hepatic tumors.

Many other water gavage studies of hydrazine sulfate in mice have resulted in increased incidence of lung adenomas/carcinomas. Strains tested included BALB/c (Biancifiori and Ribacchi, 1962), CBA/Cb/Se (Biancifiori et al., 1964; Severi and Biancifiori, 1968), BALB/c x DBA/2 (Kelly et al., 1969) and Swiss (Roe et al., 1967). Hepatomas and hepatocarcinomas were also observed in some strains as a consequence of treatment. Cb/Se rats gavaged with 18 (males) or 12 (females) mg hydrazine sulfate/day showed an increased incidence of lung tumors in both sexes and hepatomas in males only (Severi and Biancifiori, 1968).

Toth (1969) administered 0.012% hydrazine sulfate in the drinking water to

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groups of 6-week old Swiss, C3H, and AKR mice (40 to 50/sex) for their lifetimes. Groups of 110 Swiss mice and 30 C3H and AKR mice of each sex served as untreated controls. Lung adenomas and adenocarcinomas were reported in 46-50% of the treated Swiss mice (25/50 males and 24/50 females), compared with 9-11% in the controls (11/110 males and 14/110 females). Hydrazine sulfate did not induce significantly increased incidence of tumors at other sites in the Swiss mice, or at any site in the C3H or AKR mice. In a later study, Toth (1972) administered 0.001% hydrazine continuously in the drinking water to 50 Swiss mice/sex for their lifetimes. Lung adenomas and adenocarcinomas were induced in 24/50 of the males and 27/50 of the females (48-54%). Yamamoto and Weisburger (1970) reported a 100% induction of lung adenomas and adenocarcinomas (38/38 by comparison with 12/20 in the controls) in A/J male mice given 325 mg/L hydrazine sulfate in the drinking water for 48 weeks.

MacEwen et al. (1981) reported on the carcinogenic effect of inhaled hydrazine in C57BL/6 mice, F344 rats, Syrian golden hamsters and beagle dogs. Hydrazine vapor (97% pure) was administered to 400 female mice at 0.05, 0.25 or 1.0 ppm; to 100 rats of each sex at 0.05, 0.25, 1.0, or 5.0 ppm; to 160 male hamsters at 0.25, 1.0 or 5.0 ppm; and to 4 dogs of each sex at 0.25 or 1.0 ppm. Exposure was 6 hours/day, 5 days/week for 1 year, followed by a variable observation period (12-38 months). Appropriate controls were maintained for each species. Significantly increased incidences of tumors were reported at the highest exposures administered in mice (lung adenoma), male and female rats (nasal cavity adenoma and adenocarcinoma), and hamsters (nasal cavity polyp) as well as in male and female rats treated with 1.0 ppm hydrazine (nasal cavity adenoma and adenocarcinoma). No significant increase in tumor induction was observed at the lower doses nor were treatment-related neoplasms reported in the dogs. The observation period is considered to be insufficient for dogs.

Juhasz et al. (1966) injected white mice of both genders with hydrazine (0.5 mg x 16 injections) over a period of 46 days, then observed the animals for 1 year. Mediastinum reticulum-cell sarcomas were observed in 4/34 mice, and 9/34 had myeloid leukemias. A single thymic leukemia was reported out of 60 control animals. Kelly et al. (1969) injected (BALB/c\x DBA/2)F1 male mice i.p. with a total dose of 20.8 mg hydrazine sulfate/animal (given in 8 weekly injections). Lung tumors were reported in 6/30 of the treated animals and 1/9 of the control animals.

___II.A.4. SUPPORTING DATA FOR CARCINOGENICITY

The mutagenicity of hydrazine has been demonstrated in both in vitro and in vivo assays tested as hydrazine sulfate, hydrazine hydrate or hydrazine hydrochloride. Hydrazine induced reverse mutations in histidine auxotrophs of S. typhimurium (Kimball, 1977; Anderson and Styles, 1978; McMahon et al., 1979; Tosk et al., 1979; Parodi et al., 1981; Rogan et al., 1982), in tryptophan auxotrophs of E. coli (McMahon et al., 1979; Von Wright and Tikkanen, 1980), and in a host-mediated assay with mice given a single dose of hydrazine sulfate by gavage (Simmon et al., 1979). Intraperitoneal treatment of mice with hydrazine sulfate and radiolabeled formate or methionine produced radiolabeled 7-methylguanine in liver DNA and RNA, indicating that hydrazine mediated indirect alkylation of nucleic acids in vivo (Quintero-Ruiz et al., 1970). Hydrazine induces DNA strand breaks in rat hepatocytes treated in vitro (Sina et al., 1983) and in the liver and lung of mice treated intraperitoneally with hydrazine hydrate (Parodi et al., 1981). sister chromatid exchange was induced by in vitro treatment with hydrazine in Chinese hamster V-79 cells (Speit et al., 1980), Chinese hamster ovary cells (MacRae and Stitch, 1979), and Chinese hamster Don (lung) cells (Baker et al., 1983). Hydrazine induced specific locus and recessive lethal mutations in D.

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melanogaster (Jain and Shukla, 1972; Shukla, 1972) but did not induce dominant lethal mutations in mice (Epstein and Shafner, 1968; Epstein et al., 1972).

II.B. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM ORAL EXPOSUR

II.B.1. SUMMARY OF RISK ESTIMATES

Oral Slope Factor -- 3.0 per (mg/kg)/day

Drinking Water Unit Risk -- 8.5E-5 per (ug/L)

Extrapolation Method -- Linearized multistage procedure, extra risk

Drinking Water Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	1E+0 ug/L
E-5 (1 in 100,000)	1E-1 ug/L
E-6 (1 in 1,000,000)	1E-2 ug/L

II.B.2. DOSE-RESPONSE DATA (CARCINOGENICITY, ORAL EXPOSURE)

Tumor Type -- hepatoma
Test Animals -- mouse, CBA/Cb/Se; male
Route -- gavage (hydrazine sulfate in water)
Reference -- Biancifiori, 1970

Administered Dose (ppm)	Human Equivalent Dose (mg/kg)/day	Tumor Incidence
0	0	3/30
0.14	0.044	1/26
0.28	0.103	7/25
0.56	0.222	12/25
1.13	0.403	15/25

II.B.3. ADDITIONAL COMMENTS (CARCINOGENICITY, ORAL EXPOSURE)

Human equivalent doses were calculated to reflect a treatment period of 175 days and an experimental period of 607 days, the mean length of the experiment for each treatment group. Mouse body weight was assumed to be 0.03 kg and the animal lifespan was assumed to be 730 days. A slope factor of 9.01E-1 per (mg/kg)/day was derived from the lung tumor response in male Swiss mice in the single-dose lifetime drinking water study with 0.012% (0.74

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mg/day) hydrazine sulfate (Toth, 1969). The values for hydrazine would be expected to be less than these values for hydrazine sulfate because of the smaller molecular weight of the molecule. Although it is likely that hydrazine is responsible for the tumorigenic response in these experiments, the slope factor calculated on the basis of this compound may not be appropriate for hydrazine, even after converting the dose rate from hydrazine sulfate to that of hydrazine. The absorption rates in the body are likely to differ between the two compounds. The lifetime drinking water study with hydrazine in Swiss mice (Toth, 1972) is inappropriate for the calculation of a slope factor because of the lack of concurrent controls.

The unit risk should not be used if the water concentration exceeds 1E+2 ug/L, since above this concentration the unit risk may not be appropriate.

___II.B.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, ORAL EXPOSURE)

The study showed a dose-response and encompassed the lifespan of the animal. Two independent slope factors are within a factor of 4.

__II.C. QUANTITATIVE ESTIMATE OF CARCINOGENIC RISK FROM INHALATION EX

___II.C.1. SUMMARY OF RISK ESTIMATES

Inhalation Unit Risk -- 4.9E-3 per (ug/cu.m)

Extrapolation Method -- Linearized multistage procedure, extra risk

Air Concentrations at Specified Risk Levels:

Risk Level	Concentration
E-4 (1 in 10,000)	2E-2 ug/cu.m
E-5 (1 in 100,000)	2E-3 ug/cu.m
E-6 (1 in 1,000,000)	2E-4 ug/cu.m

___II.C.2. DOSE-RESPONSE DATA (CARCINOGENICITY, ORAL EXPOSURE)

Tumor Type -- nasal cavity adenoma or adenocarcinoma
Test Animals -- rat/F344, male
Route -- inhalation (hydrazine)
Reference -- MacEwen et al., 1981

---- Dose -----		Tumor
Admin-istered	Human Equivalent	Incidence

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(ppm)	(mg/kg/day)	
0.0	0.00	0/149
1.0	0.01	11/98
5.0	0.05	72/99

___II.C.3. ADDITIONAL COMMENTS (CARCINOGENICITY, INHALATION EXPOSURE)

Data in Section II.C.2. were described in the Evaluation of the Potential Carcinogenicity of Hydrazine (U.S. EPA, 1986). Global 82 was used to calculate a slope factor of 1.7E+1 per (mg/kg)/day, which was the basis for the inhalation unit risk.

Human equivalent doses reflect a treatment period of 365 days and an experimental period of 910 days. Rat body weight was assumed to be 350 g, and the animal lifespan was assumed to be 910 days.

The unit risk should not be used if the air concentration exceeds 2 ug/cu.m, since above this concentration the unit risk may not be appropriate.

___II.C.4. DISCUSSION OF CONFIDENCE (CARCINOGENICITY, INHALATION EXPOSU

A sufficient number of animals were treated for less than lifetime and observed until death; a dose-related increase in incidence was observed.

__II.D. EPA DOCUMENTATION, REVIEW, AND CONTACTS (CARCINOGENICITY ASSE

___II.D.1. EPA DOCUMENTATION

Source Document -- U.S. EPA, 1984, 1986

The values in the 1986 Reportable Quantity Document for Hydrazine (review draft) have received limited Agency review. The values in the 1984 Health and Environmental Effects Profile for Hydrazine and Hydrazine Sulfate (final draft) have received Agency review.

___II.D.2. REVIEW (CARCINOGENICITY ASSESSMENT)

Agency Work Group Review -- 06/03/87

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Verification Date -- 06/03/87

___II.D.3. U.S. EPA CONTACTS (CARCINOGENICITY ASSESSMENT)

Please contact the Risk Information Hotline for all questions concerning this assessment or IRIS, in general, at (513)569-7254 (phone), (513)569-7159 (FAX) or RIH.IRIS@EPAMAIL.EPA.GOV (internet address).

_VI. BIBLIOGRAPHY

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2
Last Revised -- 02/01/91

__VI.A. ORAL RfD REFERENCES

None

__VI.B. INHALATION RfD REFERENCES

None

__VI.C. CARCINOGENICITY ASSESSMENT REFERENCES

Anderson, D. and J.A. Styles. 1978. An evaluation of four short-term tests for detecting organic chemical carcinogens. Appendix 2. The bacterial mutation test. Br. J. Cancer. 37: 924-930.

Baker, R.S.U., G.A. Mitchell, K.M. Meher-Homji and E. Podobna. 1983. Sensitivity of two Chinese hamster cell lines to SCE induction by a variety of chemical mutagens. Mutat. Res. 118(1-2): 103-116.

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Biancifiori, C. 1970. Hepatomas in CBA/Cb/Se mice and liver lesions in golden hamsters induced by hydrazine sulfate. J. Natl. Cancer Inst. 44: 943.

Biancifiori, C. and R. Ribacchi. 1962. Pulmonary tumors in mice induced by oral isoniazid and its metabolites. Nature. 194: 488-489.

Biancifiori, C., E. Bucciarelli, D.B. Clayson and F.E. Santilli. 1964. Induction of hepatomas in CBA/Cd/Se mice by hydrazine sulphate and the lack of effect of croton oil on tumor induction in BALB/c/Cd/Se mice. Br. J. Cancer. 18: 543-550.

Epstein, S.S. and H. Shafner. 1968. Chemical mutagens in the human environment. Nature. 219: 385-387.

Epstein, S.S., E. Arnold, J. Andrea, W. Bass and Y. Bishop. 1972. Detection of chemical mutagens by the dominant lethal assay in the mouse. Toxicol. Appl. Pharmacol. 23: 288-325.

Jain, H.K. and P.T. Shukla. 1972. Locus specificity of mutagens in Drosophila. Mutat. Res. 14: 440-442.

Juhasz, J., J. Balo and B. Szende. 1966. Tumor-inducing effects of hydrazine in mice. Nature. 121: 1377.

Kelly, M.G., R.W. O'Gara, S.T. Yancey, K. Gadekar, C. Botkin and V.T. Oliverio. 1969. Comparative carcinogenicity of N-isopropyl-alpha- (2-methylhydrazine)-p-toluamide-HCl (procarbazine hydrochloride), its degradation products, other hydrazines, and isonicotinic acid hydrazine. J. Natl. Cancer Inst. 42: 337-344.

Kimball, R.F. 1977. The mutagenicity of hydrazine and some of its derivatives. Mutat. Res. 39(2): 11-126.

MacEwen, J.D., E.H. Vernot, C.C. Haun, E.R. Kinkead and A. Hall, III. 1981. Chronic Inhalation Toxicity of Hydrazine: Oncogenic Effects. Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio. NTIS, Springfield, VA.

MacRae, W.D. and H.F. Stich. 1979. Induction of sister-chromatid exchanges in Chinese hamster ovary cells by thiol and hydrazine compounds. Mutat. Res. 68(4): 351-366.

McMahon, R.E., J.C. Cline and C.Z. Thompson. 1979. Assay of 855 test chemicals in ten tester strains using a new modification of the Ames test for bacterial mutagens. Cancer Res. 39(3): 682-693.

Parodi, S., S. DeFlora, M. Cavanna, et al. 1981. DNA-damaging activity in vitro and bacterial mutagenicity of 16 hydrazine derivatives as related quantitatively to their carcinogenicity. Cancer Res. 41(4): 1469-1482.

Quintero-Ruiz, A., L.L. Paz-Neri and S. Villa-Trevino. 1981. Indirect alkylation of CBA mouse live DNA and RNA by hydrazine in vivo. A possible mechanism of action as a carcinogen. J. Natl. Cancer Inst. 67(3): 613-618.

Roe, F.J.C., G.A. Grant and D.M. Millican. 1967. Carcinogenicity of hydrazine and 1,1-dimethylhydrazine for mouse lung. Nature (London). 216: 375-376.

Roe, F.J.C. 1978. Letter to the Editor. Ann. Occup. Hyg. 21: 323-325.

Rogan, E.G., B.A. Walker, R. Gingell, D.L. Nagel and B. Toth. 1982. Microbial mutagenicity of selected hydrazines. Mutat. Res. 102(4): 413-424.

Severi, L. and C. Biancifiori. 1968. Hepatic carcinogenesis in CBA/Cb/Se

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mice and Cb/Se rats by isonicotinic acid hydrazine and hydrazone sulfate. J. Natl. Cancer Inst. 41: 331-340.

Shukla, P.T. 1972. Analysis of mutagen specificity in Drosophila melanogaster. Mutat. Res. 16: 363-371.

Simmon, V.F., H.S. Rosenkranz, E. Zeiger and L.A. Poirier. 1979. Mutagenic activity of chemical carcinogens and related compounds in the intraperitoneal host-mediated assay. J. Natl. Cancer Inst. 62(4): 911-918.

Sin, J.F., C.L. Bean, G.R. Dysart, V.I. Taylor and M.O. Bradley. 1983. Evaluation of the alkaline elution/rat hepatocyte assay as a predictor of carcinogenic/mutagenic potential. Mutat. Res. 113(5): 357-391.

Speit, G., C. Wick and M. Wolf. 1980. Induction of sister chromatid exchanges by hydroxylamine, hydrazine and isoniazid and their inhibition by cysteine. Human Genet. 52(2): 155-158.

Tosk, J., I. Schemeltz and D. Hoffman. 1979. Hydrazines as mutagens in a histidine-requiring auzotroph of Salmonella typhimurium. Mutat. Res. 66(3): 247-252.

Toth, B. 1969. Lung tumor induction and inhibition of breast adenocarcinomas by hydrazine sulfate in mice. J. Natl. Cancer Inst. 42: 469-475.

Toth, B. 1972. Hydrazine, methylhydrazine and methylhydrazine sulfate carcinogenesis in Swiss mice. Failure of ammonium hydroxide to interfere in the development of tumors. Int. J. Cancer. 9: 109-118.

U.S. EPA. 1984. Health and Environmental Effects Profile for Hydrazine and Hydrazine Sulfate. Prepared by the Office of Health and Environmental Assessment, Environmental Criteria and Assessment Office, Cincinnati, OH for the Office of Solid Waste and Emergency Response, Washington, DC.

U.S. EPA. 1986. Evaluation of the Potential Carcinogenicity of Hydrazine. Prepared by the Carcinogen Assessment Group, Office of Health and Environmental Assessment, Washington, DC for the Office of Emergency and Remedial Response and the Office of Solid Waste and Emergency Response, Washington, DC.

Von Wright, A. and L. Tikkanen. 1980. Hydrazine and methylhydrazine as recA+-independent mutagens in Escherichia coli. Mutat. Res. 71(2): 269-271.

Yamamoto, R.S. and J.H. Weisburger. 1970. Failure of arginine glutamate to inhibit lung rumor formation by isoniazid and hydrazine in mice. Life Sci. 9: 285.

_VII. REVISION HISTORY

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2

Date	Section	Description

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09/07/88	II.	Carcinogen summary on-line
04/01/89	V.	Supplementary data on-line
06/01/89	II.D.3.	Secondary contact deleted
12/01/89	II.A.3.	2nd para, deleted Biancifiori et al., 1968
12/01/89	VI.	Bibliography on-line
01/01/91	II.	Text edited
01/01/91	II.C.1.	Inhalation slope factor removed (global change)
02/01/91	II.C.3.	Information on extrapolation process included
02/01/91	II.D.1.	Title corrected for U.S. EPA, 1986
02/01/91	VI.C.	Title corrected for U.S. EPA, 1986
04/01/91	II.	Text edited
01/01/92	IV.	Regulatory Action section on-line

VIII. SYNONYMS

Substance Name -- Hydrazine/Hydrazine sulfate
CASRN -- 302-01-2
Last Revised -- 09/07/88

302-01-2
hydrazine
hydrazine, anhydrous
Hydrazine/Hydrazine sulfate

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URL: http://www.epa.gov/ngispg

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Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000.0			
-- -- -- -- 100.0	• LC_{50} (hamsters) (270 mg/m^3) • LC_{50} (mice) (106 mg/m^3)		4 4
-- -- -- -- 10.0	• LC_{50} (rats) (64 mg/m^3)		4
-- -- -- -- 1.0			
-- -- -- -- 0.1		• OSHA PEL and MSHA standard (0.35 mg/m^3)	4
-- -- -- -- 0.01		• NIOSH REL (0.08 mg/m^3) • ACGIH TLV (0.02 mg/m^3)	4 4

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
MSHA--Mine Safety and Health Administration.
NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. U.S. Environmental Protection Agency. *Health and Environmental Effects Profile for Methylhydrazine*. EPA/600/x-84/142. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.
2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online

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METHYLHYDRAZINE

Hazard Summary

- Acute (short-term) inhalation exposure to high levels of methylhydrazine may cause **lacrimation, eye redness, nasal and respiratory irritation, headache, malaise, vomiting, diarrhea, ataxia, anoxia, cyanosis, tremors, and convulsions** in humans. Acute exposure to methylhydrazine in humans has also been observed to affect the blood, kidneys, and liver. Methylhydrazine is **highly corrosive** and irritating to the skin, eyes, and mucous membranes of the respiratory system.
- Chronic (long-term) inhalation exposure to methylhydrazine has been observed to **impair function of the kidneys and liver, affect the blood and spleen, and cause convulsions** in animals.
- The Reference Concentration (RfC) for methylhydrazine is under review by the U.S. Environmental Protection Agency (EPA).
- EPA has not established a Reference Dose (RfD) for methylhydrazine.
- No information is available on the reproductive or developmental effects of methylhydrazine in humans. Reproductive effects, including changes in the morphology of sperm, have been reported in mice orally exposed to methylhydrazine.
- Information on the carcinogenic effects of methylhydrazine in humans is not available and limited animal data are available. In one study, an increased incidence of liver tumors and tumors of the cecum were observed in hamsters exposed to methylhydrazine in drinking water. However, several other studies of orally exposed rodents did not report increased incidences of tumors. EPA has classified methylhydrazine as a Group B2, **probable human carcinogen of medium carcinogenic hazard,** with a $1/ED_{10}$ value of 4.1 per (mg/kg)/d.[a]

[a] The $1/ED_{10}$ value is a measure of the carcinogenic potency of a chemical. The value reported here has been proposed in the hazard ranking of hazardous air pollutants in EPA's proposed rulemaking (Section 112(g) of the Clean Air Act, April 1994).

Please Note: The main sources of information for this fact sheet are EPA's *Health and Environmental Effects Profile for Methylhydrazine* and the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature. Other secondary sources include Sittig's *Handbook of Toxic and Hazardous Chemicals and Carcinogens* and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Individuals may be exposed to methylhydrazine in the ambient atmosphere during its use as rocket fuel, and from spills, leaks, and venting during loading, transfer, and storage. (1)
- Individuals may be exposed to methylhydrazine in the workplace.
- Exposure to methylhydrazine may occur through the consumption of a species of edible mushroom. (2)

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Assessing Personal Exposure

- No information was located concerning the measurement of personal exposure to methylhydrazine.

Health Hazard Information

Acute Effects:

- Acute (short-term) inhalation exposure to high levels of methylhydrazine may cause lacrimation, eye redness, nasal and respiratory irritation, headache, malaise, vomiting, diarrhea, ataxia, anoxia, cyanosis, tremors, and convulsions in humans. (1-3)
- Methemoglobin formation and damage to the kidneys and liver may also occur following acute exposure. (1)
- Fatal hepatic necrosis developed following acute exposure of humans by ingestion of poisonous mushrooms containing methylhydrazine. (2)
- Acute exposure of humans to methylhydrazine by inhalation causes effects on the blood, including hemolytic anemia and the destruction of red blood cells. (1,2)
- Methylhydrazine is highly corrosive and irritating to the skin, eyes, and mucous membranes of the respiratory system. (2,3)
- Methemoglobin formation and damage to the kidneys and liver has been reported in one study following acute percutaneous administration of methylhydrazine in dogs. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, hamsters, and guinea pigs, have demonstrated methylhydrazine to have high acute toxicity from inhalation exposure, extreme acute toxicity from oral exposure, and high to extreme acute toxicity from dermal exposure. (4)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, considers methylhydrazine to be a "high concern" pollutant based on severe acute toxicity. (5)

Chronic Effects (Noncancer):

- Chronic (long-term) inhalation exposure to methylhydrazine has been observed to impair function of the kidneys and liver, affect the blood and spleen, and cause convulsions in animals. (1)
- The RfC for methylhydrazine is under review by EPA. (6)
- EPA has not established an RfD for methylhydrazine. (6)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of methyl-hydrazine in humans.
- Malformations have not been observed in the offspring of rats orally exposed to methylhydrazine, while malformations were reported in the toad. (1,2)
- The morphology of sperm has been reported to be affected in mice orally exposed to methylhydrazine. (1,2)

Cancer Risk:

- No information is available on the carcinogenic effects of methylhydrazine in humans.
- In one study, an increased incidence of liver tumors and tumors of the cecum were observed in hamsters exposed to methylhydrazine in drinking water. However, several other studies of orally exposed rodents did not report increased incidences of tumors. (1,2)

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- EPA considers methylhydrazine to be a probable human carcinogen (cancer-causing agent) and has classified it as a Group B2 carcinogen. (5)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has ranked methylhydrazine in the nonthreshold category. The $1/ED_{10}$ value is 4.1 per (mg/kg)/d and this would place it in the medium category under Superfund's ranking for carcinogenic hazard. (5)

Physical Properties

- The chemical formula for methylhydrazine is CH_6N_2, and its molecular weight is 46.1 g/mol. (1,7)
- Methylhydrazine is a colorless, flammable liquid that is miscible with water. (1)
- Methylhydrazine has an ammonia-like fishy smell with an odor threshold of 1.7 ppm. (1,8)
- The vapor pressure for methylhydrazine is 49.6 mm Hg at 25 C, and its log octanol/water partition coefficient (log K_{ow}) is -1.50. (1,2)

Uses

- Methylhydrazine is primarily used as a high-energy fuel in military applications, as a rocket propellant and fuel for thrusters, and as fuel for small electrical power generating units. (1,2,7)
- Methylhydrazine is also used as a chemical intermediate and as a solvent. (2,7)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45).

For methylhydrazine: 1 ppm = 1.88 mg/m^3.

Health Data from Inhalation Exposure

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database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
3. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
5. U.S. Environmental Protection Agency. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health*. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.
6. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Methylhydrazine*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
7. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
8. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

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ToxFAQs

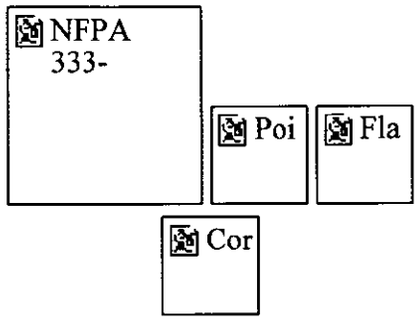
Hydrazines

CAS# 302-01-2, 57-14-7, 540-73-8

September 1997

Hydrazine
H_4N_2
Stereo Image
XYZ File

ChemFinder

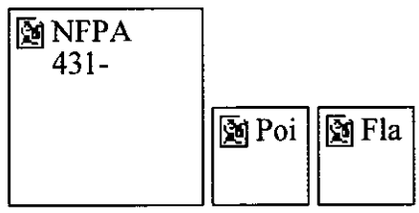


NFPA Label Key

Material Safety Data Sheet
(University of Utah)

1,1-Dimethylhydrazine
$C_2H_8N_2$
Stereo Image
XYZ File

ChemFinder



NFPA Label Key

1,2-Dimethylhydrazine
$C_2H_8N_2$
Stereo Image
XYZ File

ChemFinder

NFPA Label Key

Agency for Toxic Substances and Disease Registry

This fact sheet answers the most frequently asked health questions (FAQs) about hydrazines. For more information, call the ATSDR Information Center at 1-800-447-1544. This fact sheet is one in a series of summaries about hazardous substances and their health effects. It's important you understand this information because these substances may harm you. The effects of exposure to any hazardous substance depend on the dose, the duration, how you are exposed, personal traits and habits, and whether other chemicals are present.

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habits, and whether other chemicals are present.

HIGHLIGHTS: Hydrazines are colorless liquids that are used in rocket fuels, chemical manufacturing, and as boiler water treatments. Exposure to hydrazines may cause nervous system effects, as well as liver and kidney damage. Hydrazines have been found in at least 8 of the 1,416 National Priorities List sites identified by the Environmental Protection Agency (EPA).

What are hydrazines?

Hydrazines are clear, colorless liquids with an ammonia-like odor. There are many kinds of hydrazine compounds, including hydrazine, 1,1-dimethylhydrazine, and 1,2-dimethylhydrazine. Small amounts of hydrazine occur naturally in plants. Most hydrazines are manufactured for use as rocket propellants and fuels, boiler water treatments, chemical reactants, medicines, and in cancer research. Hydrazines are highly reactive and easily catch fire.

What happens to hydrazines when they enter the environment?

- Hydrazines can be released into the environment during their production or use, or from accidental spills.
- Hydrazines easily evaporate to the air, where they are broken down by reactions within minutes or hours.
- Hydrazines can also dissolve in water, where they usually break down into less toxic compounds within a few weeks.
- Hydrazines may build up in some fish living in contaminated water, but are not expected to remain at high levels over long periods of time.
- In soil, hydrazines may stick to particles and be changed within a few days to less harmful compounds.

How might I be exposed to hydrazines?

- Breathing contaminated air in or near a facility that makes, processes, or uses hydrazines
- Eating fish contaminated with hydrazines
- Drinking or swimming in water that has been contaminated with hydrazines
- Touching soil contaminated with hydrazines, such as near some military bases or hazardous waste sites
- Breathing cigarette smoke indirectly or using tobacco products may expose you to small amounts of hydrazine or 1,1-dimethylhydrazine
- Working in greenhouses where the chemical Alar is used may result in your being exposed to small amounts of 1,2-dimethylhydrazine

How can hydrazines affect my health?

Breathing hydrazines for short periods may cause coughing and irritation of the throat and lungs, convulsions, tremors, or seizures. Breathing hydrazines for long periods may cause liver and kidney damage, as well as serious effects on reproductive organs.

Eating or drinking small amounts of hydrazines may cause nausea, vomiting, uncontrolled shaking, inflammation of the nerves, drowsiness, or coma.

How likely are hydrazines to cause cancer?

Tumors have been seen in many organs of animals that were exposed to hydrazines by ingestion or breathing, but most tumors have been found in the lungs, blood vessels, or colon. 1,2-Dimethylhydrazine has caused colon cancer in laboratory animals following a single exposure.

The **Department of Health and Human Services (DHHS)** has determined that hydrazine and

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The **Department of Health and Human Services (DHHS)** has determined that hydrazine and 1,1-dimethylhydrazine are known carcinogens.

The **International Agency for Research on Cancer (IARC)** has determined that hydrazine, 1,1-dimethylhydrazine, and 1,2-dimethylhydrazine are possible human carcinogens.

The **EPA** has determined that hydrazine, 1,1-dimethylhydrazine, and 1,2-dimethylhydrazine are probable human carcinogens.

The **American Conference of Governmental Industrial Hygienists (ACGIH)** currently lists hydrazine and 1,1-dimethylhydrazine as suspected carcinogens, but has recently recommended that the listing of hydrazine be changed to that of animal carcinogen, not likely to cause cancer to people under normal exposure conditions.

Is there a medical test to show whether I've been exposed to hydrazines?

There are tests available to detect the presence of hydrazines or their breakdown products in the blood, urine, and feces. These tests must be done soon after exposure, before the compounds are broken down and eliminated from the body. These tests aren't available at most doctors' offices, but can be done at special laboratories that have the right equipment. These tests cannot be used to tell how much hydrazines you were exposed to or if any health effects will occur.

Has the federal government made recommendations to protect human health?

The **National Institute for Occupational Safety and Health (NIOSH)** recommends that the levels of hydrazine and 1,1-dimethylhydrazine in workplace air not exceed 0.03 and 0.6 parts of compound per million parts of air (0.03–0.6 ppm), respectively, for a 2-hour period.

The **Occupational Safety and Health Administration (OSHA)** limits the amount of hydrazine and 1,1-dimethylhydrazine in workplace air to 1 and 0.5 ppm, respectively, for an 8-hour workday.

The **Food and Drug Administration (FDA)** has ruled that hydrazine cannot be added to water used for making steam which will contact food. The **EPA** requires that spills or accidental releases into the environment of 1 pound or more of hydrazine or 1,2-dimethylhydrazine, or more than 10 pounds of 1,1-dimethylhydrazine be reported to the **EPA**.

Glossary

Carcinogen:
A substance with the ability to cause cancer
CAS:
Chemical Abstracts Service
Evaporate:
To change into a vapor or gas
Ingest:
To eat or drink something
PPM:
Parts per million

Source of Information

This ToxFAQs information is taken from the 1997 Toxicological Profile for Hydrazines produced by the Agency for Toxic Substances and Disease Registry, Public Health Service, U.S. Department of Health and Human Services, Public Health Service in Atlanta, GA.

Animal testing is sometimes necessary to find out how toxic substances might harm people and how to treat people who have been exposed. Laws today protect the welfare of research animals and scientists

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must follow strict guidelines.

Where can I get more information?

ATSDR can tell you where to find occupational and environmental health clinics. Their specialists can recognize, evaluate, and treat illnesses resulting from exposure to hazardous substances. You can also contact your community or state health or environmental quality department if you have any more questions or concerns.

For more information, contact:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road NE, Mailstop E-29
Atlanta, GA 30333
Phone: 1-800-447-1544
Fax: 404-639-6359

U.S. Department of Health and Human Services
Public Health Service
Agency for Toxic Substances and Disease Registry

Link to ToxFAQs Home Page

Link to ATSDR Science Corner

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HYDRAZINE

302-01-2

Hazard Summary

- Symptoms of acute (short-term) exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and central nervous system in humans. The liquid is corrosive and may produce **chemical burns and severe dermatitis** from skin contact.
- Information is not available on the chronic (long-term) effects of hydrazine in humans. In rats chronically exposed to hydrazine by inhalation, inflammatory changes of the respiratory tract were observed. In another chronic inhalation study, rats demonstrated depressed growth rates, liver damage occurred in mice, and fatty changes in the liver and spleen were reported in dogs.
- The U.S. Environmental Protection Agency (EPA) has not established a Reference Concentration (RfC) or a Reference Dose (RfD) for hydrazine.
- Information is not available on the reproductive or developmental effects of hydrazine in humans. Hydrazine is **fetotoxic to rodents** exposed by injection. Reduced ratio of fetal survivors to implantation sites, reduced fetal weight, and generalized edema, but no gross malformations were observed in rats.
- Adequate information is not available on the carcinogenic effects of hydrazine in humans. Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. EPA has classified hydrazine as a Group B2, **probable human carcinogen of high carcinogenic hazard**, with a $1/ED_{10}$ value of 107 per (mg/kg)d[a] and an inhalation unit risk estimate of 4.9×10^{-3} $(g/m^3)^{-1}$.

[a] The $1/ED_{10}$ value is a measure of the carcinogenic potency of a chemical. The value reported here has been proposed in the hazard ranking of hazardous air pollutants in EPA's proposed rulemaking (Section 112(g) of the Clean Air Act, April 1994).

Please Note: The main sources of information for this fact sheet are EPA's Integrated Risk Information System (IRIS), which contains information on the carcinogenic effects of hydrazine including the unit cancer risk for inhalation exposure, and EPA's *Health and Environmental Effects Profile for Hydrazine*. Other secondary sources include the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature, and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Individuals may be occupationally exposed to hydrazine in the workplace. (1,2)
- Accidental discharge into water, air, and soil may occur during storage, handling, transport, and improper waste disposal. However, hydrazine rapidly degrades in the environment and is rarely encountered. (2,3)

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- Hydrazine has been detected in tobacco smoke. (2)

Assessing Personal Exposure

- Hydrazine may be detected in the blood of exposed individuals. (1,2)

Health Hazard Information

Acute Effects:

- Symptoms of acute (short-term) exposure to high levels of hydrazine include irritation of the eyes, nose, and throat, temporary blindness, dizziness, headache, nausea, pulmonary edema, seizures, and coma in humans. Acute exposure can also damage the liver, kidneys, and CNS in humans. (2-4)
- The liquid is corrosive and may produce chemical burns and severe dermatitis from skin contact. (1,4)
- Acute animal tests, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, and guinea pigs, have demonstrated hydrazine to have high acute toxicity from inhalation and ingestion and extreme acute toxicity from dermal exposure. (5)

Chronic Effects (Noncancer):

- Information is not available on the chronic (long-term) effects of hydrazine in humans.
- In rats chronically exposed to hydrazine by inhalation, inflammatory changes of the respiratory tract were observed. In another chronic inhalation study, rats demonstrated depressed growth rates, liver damage occurred in mice, and fatty changes in the liver and spleen were reported in dogs. (6)
- EPA has not established an RfC or an RfD for hydrazine. (4)

Reproductive/Developmental Effects:

- Information is not available on the reproductive or developmental effects of hydrazine in humans.
- Hydrazine is fetotoxic to rodents exposed by injection. Reduced ratio of fetal survivors to implantation sites, reduced fetal weight, and no gross malformations, but generalized edema, were observed in rats. (6)

Cancer Risk:

- Adequate information is not available on the carcinogenic effects of hydrazine in humans.
- Increased incidences of lung and liver tumors have been observed in mice exposed to hydrazine by inhalation, in their drinking water, via gavage and injection. Tumors in the nasal cavity were observed in rats and hamsters exposed by inhalation. (4,6,7)
- EPA has classified hydrazine as a Group B2, probable human carcinogen. (4)
- EPA uses mathematical models, based on human and animal studies, to estimate the probability of a person developing cancer from breathing air containing a specified concentration of a chemical. EPA calculated an inhalation unit risk estimate of 4.9×10^{-3} $(g/m^3)^{-1}$. EPA estimates that, if an individual were to breathe air containing hydrazine at 0.0002 g/m^3(1) over his or her entire lifetime, that person would theoretically have no more than a one-in-a-million increased chance of developing cancer as a direct result of breathing air containing this chemical. Similarly, EPA estimates that breathing air containing 0.002 $\mu g/m^3$ would result in not greater than a one-in-a-hundred thousand increased chance of developing cancer, and air containing 0.02 $\mu g/m^3$ would result in not greater than a one-in-ten thousand increased chance of developing cancer. (4)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of

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the Clean Air Act Amendments, has ranked hydrazine in the nonthreshold category. The $1/ED_{10}$ value is 107 per (mg/kg)/d and this would place it in the high category under Superfund's ranking for carcinogenic hazard. ( )

Physical Properties

- The chemical formula for hydrazine is H_4N_2, and its molecular weight is 32.05 g/mol. (6)
- Hydrazine occurs as a colorless, oily, flammable liquid that is miscible with water. (6,8)
- Hydrazine has a penetrating odor, resembling that of ammonia, with an odor threshold of 3.7 ppm. (8,9)
- The vapor pressure for hydrazine is 14.4 mm Hg at 25 C, and its log octanol/water partition coefficient (log K_{ow}) is 0.08. (6)

Uses

- Hydrazine is used in agricultural chemicals (pesticides), blowing agents, pharmaceutical intermediates, photography chemicals, water treatment for corrosion protection, textile dyes, and jet and rocket fuel. (4,6,8)

Conversion Factors:
To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45). For hydrazine: 1 ppm = 1.31 mg/m^3.

Health Data from Inhalation Exposure

Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000.0			
-- -- -- -- 100.0	• LC_{50} (rats) (747 mg/m^3) • LC_{50} (mice) (330 mg/m^3)		5 5
-- -- -- -- 10.0			
-- -- -- -- 1.0		• MSHA standard (1.3 mg/m^3)	5
-- -- -- -- 0.1		• OHSA PEL (0.1 mg/m^3)	5

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-- -- -- -- 0.01		• ACGIH TLV (0.01 mg/m^3)	5
-- -- -- -- 0.001			
-- -- -- -- 0.0001			
-- -- -- -- 0.00001			
-- -- -- -- 0.000001			
-- -- -- -- 0.0000001	• EPA Cancer Risk Level (1-in-a-million excess lifetime risk) = 2.0×10^{-7} mg/m^3		3

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal Concentration$_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
MSHA--Mine Safety and Health Administration.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens.* 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
2. World Health Organization. *Environmental Health Criteria 68: Hydrazine.* Geneva, Switzerland. 1987.
3. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online database). National Toxicology Information Program, National Library of Medicine, Bethesda,

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MD. 1993.
4. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Hydrazine/Hydrazine Sulfate*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
5. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
6. U.S. Environmental Protection Agency. *Health and Environmental Effects Profile for Hydrazine and Hydrazine Sulfate*. EPA/600/x-84/332. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.
7. International Agency for Research on Cancer (IARC). *IARC Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man: Some Aromatic Amines, Hydrazine and Related Substances, N-Nitroso Compounds and Miscellaneous Alkylating Agents*. Volume 4. World Health Organization, Lyon. 1974.
8. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
9. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

1. *Micrograms per cubic meter is the unit of measurement for chemicals in air.

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METHYLHYDRAZINE

Hazard Summary

- Acute (short-term) inhalation exposure to high levels of methylhydrazine may cause **lacrimation, eye redness, nasal and respiratory irritation, headache, malaise, vomiting, diarrhea, ataxia, anoxia, cyanosis, tremors, and convulsions** in humans. Acute exposure to methylhydrazine in humans has also been observed to affect the blood, kidneys, and liver. Methylhydrazine is **highly corrosive** and irritating to the skin, eyes, and mucous membranes of the respiratory system.
- Chronic (long-term) inhalation exposure to methylhydrazine has been observed to **impair function of the kidneys and liver, affect the blood and spleen, and cause convulsions** in animals.
- The Reference Concentration (RfC) for methylhydrazine is under review by the U.S. Environmental Protection Agency (EPA).
- EPA has not established a Reference Dose (RfD) for methylhydrazine.
- No information is available on the reproductive or developmental effects of methylhydrazine in humans. Reproductive effects, including changes in the morphology of sperm, have been reported in mice orally exposed to methylhydrazine.
- Information on the carcinogenic effects of methylhydrazine in humans is not available and limited animal data are available. In one study, an increased incidence of liver tumors and tumors of the cecum were observed in hamsters exposed to methylhydrazine in drinking water. However, several other studies of orally exposed rodents did not report increased incidences of tumors. EPA has classified methylhydrazine as a Group B2, **probable human carcinogen of medium carcinogenic hazard,** with a $1/ED_{10}$ value of 4.1 per (mg/kg)/d.[a]

[a] The $1/ED_{10}$ value is a measure of the carcinogenic potency of a chemical. The value reported here has been proposed in the hazard ranking of hazardous air pollutants in EPA's proposed rulemaking (Section 112(g) of the Clean Air Act, April 1994).

Please Note: The main sources of information for this fact sheet are EPA's *Health and Environmental Effects Profile for Methylhydrazine* and the Hazardous Substances Data Bank (HSDB), a database of summaries of peer-reviewed literature. Other secondary sources include Sittig's *Handbook of Toxic and Hazardous Chemicals and Carcinogens* and the Registry of Toxic Effects of Chemical Substances (RTECS), a database of toxic effects that are not peer reviewed.

Environmental/Occupational Exposure

- Individuals may be exposed to methylhydrazine in the ambient atmosphere during its use as rocket fuel, and from spills, leaks, and venting during loading, transfer, and storage. (1)
- Individuals may be exposed to methylhydrazine in the workplace.
- Exposure to methylhydrazine may occur through the consumption of a species of edible mushroom. (2)

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Assessing Personal Exposure

- No information was located concerning the measurement of personal exposure to methylhydrazine.

Health Hazard Information

Acute Effects:

- Acute (short-term) inhalation exposure to high levels of methylhydrazine may cause lacrimation, eye redness, nasal and respiratory irritation, headache, malaise, vomiting, diarrhea, ataxia, anoxia, cyanosis, tremors, and convulsions in humans. (1-3)
- Methemoglobin formation and damage to the kidneys and liver may also occur following acute exposure. (1)
- Fatal hepatic necrosis developed following acute exposure of humans by ingestion of poisonous mushrooms containing methylhydrazine. (2)
- Acute exposure of humans to methylhydrazine by inhalation causes effects on the blood, including hemolytic anemia and the destruction of red blood cells. (1,2)
- Methylhydrazine is highly corrosive and irritating to the skin, eyes, and mucous membranes of the respiratory system. (2,3)
- Methemoglobin formation and damage to the kidneys and liver has been reported in one study following acute percutaneous administration of methylhydrazine in dogs. (1)
- Tests involving acute exposure of animals, such as the LC_{50} and LD_{50} tests in rats, mice, rabbits, hamsters, and guinea pigs, have demonstrated methylhydrazine to have high acute toxicity from inhalation exposure, extreme acute toxicity from oral exposure, and high to extreme acute toxicity from dermal exposure. (4)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, considers methylhydrazine to be a "high concern" pollutant based on severe acute toxicity. (5)

Chronic Effects (Noncancer):

- Chronic (long-term) inhalation exposure to methylhydrazine has been observed to impair function of the kidneys and liver, affect the blood and spleen, and cause convulsions in animals. (1)
- The RfC for methylhydrazine is under review by EPA. (6)
- EPA has not established an RfD for methylhydrazine. (6)

Reproductive/Developmental Effects:

- No information is available on the reproductive or developmental effects of methyl-hydrazine in humans.
- Malformations have not been observed in the offspring of rats orally exposed to methylhydrazine, while malformations were reported in the toad. (1,2)
- The morphology of sperm has been reported to be affected in mice orally exposed to methylhydrazine. (1,2)

Cancer Risk:

- No information is available on the carcinogenic effects of methylhydrazine in humans.
- In one study, an increased incidence of liver tumors and tumors of the cecum were observed in hamsters exposed to methylhydrazine in drinking water. However, several other studies of orally exposed rodents did not report increased incidences of tumors. (1,2)

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- EPA considers methylhydrazine to be a probable human carcinogen (cancer-causing agent) and has classified it as a Group B2 carcinogen. (5)
- EPA's Office of Air Quality Planning and Standards, for a hazard ranking under Section 112(g) of the Clean Air Act Amendments, has ranked methylhydrazine in the nonthreshold category. The $1/ED_{10}$ value is 4.1 per (mg/kg)/d and this would place it in the medium category under Superfund's ranking for carcinogenic hazard. (5)

Physical Properties

- The chemical formula for methylhydrazine is CH_6N_2, and its molecular weight is 46.1 g/mol. (1,7)
- Methylhydrazine is a colorless, flammable liquid that is miscible with water. (1)
- Methylhydrazine has an ammonia-like fishy smell with an odor threshold of 1.7 ppm. (1,8)
- The vapor pressure for methylhydrazine is 49.6 mm Hg at 25 C, and its log octanol/water partition coefficient (log K_{ow}) is -1.50. (1,2)

Uses

- Methylhydrazine is primarily used as a high-energy fuel in military applications, as a rocket propellant and fuel for thrusters, and as fuel for small electrical power generating units. (1,2,7)
- Methylhydrazine is also used as a chemical intermediate and as a solvent. (2,7)

Conversion Factors:

To convert from ppm to mg/m^3: mg/m^3 = (ppm) × (molecular weight of the compound)/(24.45).
For methylhydrazine: 1 ppm = 1.88 mg/m^3.

Health Data from Inhalation Exposure

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Concentration (mg/m^3)	Health numbers[a]	Regulatory, advisory numbers[b]	Reference
1,000.0			
-- -- -- -- 100.0	• LC_{50} (hamsters) (270 mg/m^3) • LC_{50} (mice) (106 mg/m^3)		4 4
-- -- -- -- 10.0	• LC_{50} (rats) (64 mg/m^3)		4
-- -- -- -- 1.0			
-- -- -- -- 0.1		• OSHA PEL and MSHA standard (0.35 mg/m^3)	4
-- -- -- -- 0.01		• NIOSH REL (0.08 mg/m^3) • ACGIH TLV (0.02 mg/m^3)	4 4

ACGIH TLV--American Conference of Governmental and Industrial Hygienists' threshold limit value expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effects.
LC_{50} (Lethal $Concentration_{50}$)--A calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined experimental animal population.
MSHA--Mine Safety and Health Administration.
NIOSH REL--National Institute of Occupational Safety and Health's recommended exposure limit; NIOSH-recommended exposure limit for an 8- or 10-h time-weighted-average exposure and/or ceiling.
OSHA PEL--Occupational Safety and Health Administration's permissible exposure limit expressed as a time-weighted average; the concentration of a substance to which most workers can be exposed without adverse effect averaged over a normal 8-h workday or a 40-h workweek.

[a] Health numbers are toxicological numbers from animal testing or risk assessment values developed by EPA.
[b] Regulatory numbers are values that have been incorporated in Government regulations, while advisory numbers are nonregulatory values provided by the Government or other groups as advice.

References

1. U.S. Environmental Protection Agency. *Health and Environmental Effects Profile for Methylhydrazine*. EPA/600/x-84/142. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1984.
2. U.S. Department of Health and Human Services. Hazardous Substances Data Bank (HSDB, online

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database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
3. M. Sittig. *Handbook of Toxic and Hazardous Chemicals and Carcinogens*. 2nd ed. Noyes Publications, Park Ridge, NJ. 1985.
4. U.S. Department of Health and Human Services. Registry of Toxic Effects of Chemical Substances (RTECS, online database). National Toxicology Information Program, National Library of Medicine, Bethesda, MD. 1993.
5. U.S. Environmental Protection Agency. *Technical Background Document to Support Rulemaking Pursuant to the Clean Air Act--Section 112(g). Ranking of Pollutants with Respect to Hazard to Human Health*. EPA-450/3-92-010. Emissions Standards Division, Office of Air Quality Planning and Standards, Research Triangle Park, NC. 1994.
6. U.S. Environmental Protection Agency. *Integrated Risk Information System (IRIS) on Methylhydrazine*. Environmental Criteria and Assessment Office, Office of Health and Environmental Assessment, Office of Research and Development, Cincinnati, OH. 1993.
7. *The Merck Index. An Encyclopedia of Chemicals, Drugs, and Biologicals*. 11th ed. Ed. S. Budavari. Merck and Co. Inc., Rahway, NJ. 1989.
8. J.E. Amoore and E. Hautala. Odor as an aid to chemical safety: Odor thresholds compared with threshold limit values and volatilities for 214 industrial chemicals in air and water dilution. *Journal of Applied Toxicology*, 3(6):272-290. 1983.

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HDMSP001793932

HYDRAZINE
(Group 2B)

For definition of Groups, see Preamble Evaluation.

Supplement 7: (1987) (p. 222)

CAS No.: 302-01-2

A. Evidence for carcinogenicity to humans (*inadequate*)

Two reports of cancer mortality in workers exposed to hydrazine have appeared in recent years. Choroidal melanoma was observed in one man who had been exposed to hydrazine for six years [ref: 1]. A preliminary report of an epidemiological study of men engaged in hydrazine manufacture revealed no unusual excess of cancer. This study comprised 423 men, with a 64% vital status ascertainment. None of the five cancers reported (three of the stomach, one prostatic and one neurogenic) occurred in the group with the highest exposure [ref: 2]. A follow-up study of this cohort [ref: 3] has extended it to 1982. Mortality from all causes was not elevated (49 observed, 61.47 expected), and the only excess entailed two lung cancer cases within the highest exposure category, with a relative risk of 1.2 (95% confidence interval, 0.2-4.5).

B. Evidence for carcinogenicity to animals (*sufficient*)

Hydrazine has been tested in mice by oral administration, producing liver and mammary tumours and lung tumours in both P and F_1 generations; after intraperitoneal administration to mice, it produced lung tumours, leukaemias and sarcomas [ref: 4,5]. After oral administration to rats, it produced lung and liver tumours [ref: 4]. When tested by inhalation, it produced benign and malignant nasal tumours in rats, benign nasal polyps, a few colon tumours and thyroid adenomas in hamsters, and a slight increase in the incidence of lung adenomas in mice [ref: 6].

C. Other relevant data

No data were available on the genetic and related effects of hydrazine in humans.

Hydrazine did not induce dominant lethal mutations or micronuclei in bone-marrow cells of mice treated *in vivo*. It induced unscheduled DNA synthesis in human cells *in vitro*. It did not induce chromosomal aberrations in rat cells *in vitro* but induced sister chromatid exchanges in Chinese hamster cells; conflicting results were obtained for the induction of mutation in mouse lymphoma cells. It induced DNA strand breaks in rat hepatocytes *in vitro*. Hydrazine induced somatic mutation in *Drosophila* and chromosomal aberrations and mutation in plants. It was mutagenic to yeast and bacteria and induced DNA damage in bacteria [ref: 7].

Overall evaluation

Hydrazine is *possibly carcinogenic to humans (Group 2B)*.

For definition of the italicized terms, see Preamble Evaluation.

Also see previous evaluation: Vol. 4 (1974)

References

1. Albert, D.M. & Puliafito, C.A. (1977) Choroidal melanoma: possible exposure to industrial toxins. New Engl. J. Med., 296, 634-635

2. Roe, F.J.C. (1978) Hydrazine. Ann. occup. Hyg., 21, 323-326

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3. Wald, N., Boreham, J., Doll, R. & Bonsall, J. (1984) Occupational exposure to hydrazine and subsequent risk of cancer. Br. J. ind. Med., 41, 31-34

4. IARC Monographs, 4, 127-136, 1974

5. Menon, M.M. & Bhide, S.V. (1983) Perinatal carcinogenicity of izoniazid (INH) in Swiss mice. J. Cancer Res. clin. Oncol., 105, 258-261

6. Vernot, E.H., MacEwen, J.D., Bruner, R.H., Haun, C.C., Kinkead, E.R., Prentice, D.E., Hall, A., Schmidt, R.E., Eason, R.L., Hubbard, G.B. & Young, J.T. (1985) Long-term inhalation toxicity of hydrazine. Fundam. appl. Toxicol., 5, 1050-1064

7. IARC Monographs, Suppl. 6, 341-343, 1987

Synonyms

- Diamide
- Diamine
- Hydrazine base

Last updated: 3 March 1998

BNA08768247

HDMSP001793934

HYDRAZINE

VOL.: 4 (1974) (p. 127)

5. Summary of Data Reported and Evaluation

5.1 Animal carcinogenicity data

Hydrazine or hydrazine salts have been shown to be carcinogenic in mice after oral and intraperitoneal administration, and in rats following oral administration. No tumours were observed in Syrian golden hamsters after oral administration.

5.2 Human carcinogenicity data

No epidemiological data are available to the Working Group.

Subsequent evaluation: Suppl. 7 (1987)

Last updated: 16 March 1998

BNA08768248

HDMSP001793935

1,1-DIMETHYLHYDRAZINE

VOL.: 4 (1974) (p. 137)

CAS No.: 57-14-7

5. Summary of Data Reported and Evaluation

5.1 Animal carcinogenicity data

1,1-Dimethylhydrazine (UDMH) is carcinogenic in mice after oral administration. The observation of a few liver tumours after high oral doses of UDMH occurring in rats after a long latent period does not allow a proper evaluation of the carcinogenic effect in this species.

5.2 Human carcinogenicity data

No epidemiological data are available to the Working Group.

Subsequent evaluation: Suppl. 7 (1987) (p. 62: **Group 2B)**

For definition of Groups, see Preamble Evaluation.

Synonyms

- Asymmetrical-dimethylhydrazine
- Dimazine
- Dimethylhydrazine
- *N,N*-Dimethylhydrazine
- UDMH
- UNS-dimethylhydrazine
- Unsymmetrical dimethylhydrazine

Last updated: 16 March 1998

BNA08768249

HDMSP001793936

12. Evaluation

Evaluations of the strength of the evidence for carcinogenicity arising from human and experimental animal data are made, using standard terms.

It is recognized that the criteria for these evaluations, described below, cannot encompass all of the factors that may be relevant to an evaluation of carcinogenicity. In considering all of the relevant scientific data, the Working Group may assign the agent, mixture or exposure circumstance to a higher or lower category than a strict interpretation of these criteria would indicate.

(a) Degrees of evidence for carcinogenicity in humans and in experimental animals and supporting evidence

These categories refer only to the strength of the evidence that an exposure is carcinogenic and not to the extent of its carcinogenic activity (potency) nor to the mechanisms involved. A classification may change as new information becomes available.

An evaluation of degree of evidence, whether for a single agent or a mixture, is limited to the materials tested, as defined physically, chemically or biologically. When the agents evaluated are considered by the Working Group to be sufficiently closely related, they may be grouped together for the purpose of a single evaluation of degree of evidence.

(i) *Carcinogenicity in humans*

The applicability of an evaluation of the carcinogenicity of a mixture, process, occupation or industry on the basis of evidence from epidemiological studies depends on the variability over time and place of the mixtures, processes, occupations and industries. The Working Group seeks to identify the specific exposure, process or activity which is considered most likely to be responsible for any excess risk. The evaluation is focused as narrowly as the available data on exposure and other aspects permit.

The evidence relevant to carcinogenicity from studies in humans is classified into one of the following categories:

Sufficient evidence of carcinogenicity: The Working Group considers that a causal relationship has been established between exposure to the agent, mixture or exposure circumstance and human cancer. That is, a positive relationship has been observed between the exposure and cancer in studies in which chance, bias and confounding could be ruled out with reasonable confidence.

Limited evidence of carcinogenicity: A positive association has been observed between exposure to the agent, mixture or exposure circumstance and cancer for which a causal interpretation is considered by the Working Group to be credible, but chance, bias or confounding could not be ruled out with reasonable confidence.

Inadequate evidence of carcinogenicity: The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of a causal association, or no data on cancer in humans are available.

Evidence suggesting lack of carcinogenicity: There are several adequate studies covering the full range of levels of exposure that human beings are known to encounter, which are mutually consistent in not showing a positive association between exposure to the agent, mixture or exposure circumstance and any studied cancer at any observed level of exposure. A conclusion of 'evidence suggesting lack of carcinogenicity' is inevitably limited to the cancer sites, conditions and levels of exposure and length of observation covered by the available studies. In addition, the possibility of a very small risk at the levels of exposure studied can never be excluded.

In some instances, the above categories may be used to classify the degree of evidence related to carcinogenicity in specific organs or tissues.

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(ii) *Carcinogenicity in experimental animals*

The evidence relevant to carcinogenicity in experimental animals is classified into one of the following categories:

Sufficient evidence of carcinogenicity: The Working Group considers that a causal relationship has been established between the agent or mixture and an increased incidence of malignant neoplasms or of an appropriate combination of benign and malignant neoplasms in (a) two or more species of animals or (b) in two or more independent studies in one species carried out at different times or in different laboratories or under different protocols.

Exceptionally, a single study in one species might be considered to provide sufficient evidence of carcinogenicity when malignant neoplasms occur to an unusual degree with regard to incidence, site, type of tumour or age at onset.

Limited evidence of carcinogenicity: The data suggest a carcinogenic effect but are limited for making a definitive evaluation because, e.g. (a) the evidence of carcinogenicity is restricted to a single experiment; or (b) there are unresolved questions regarding the adequacy of the design, conduct or interpretation of the study; or (c) the agent or mixture increases the incidence only of benign neoplasms or lesions of uncertain neoplastic potential, or of certain neoplasms which may occur spontaneously in high incidences in certain strains.

Inadequate evidence of carcinogenicity: The studies cannot be interpreted as showing either the presence or absence of a carcinogenic effect because of major qualitative or quantitative limitations, or no data on cancer in experimental animals are available.

Evidence suggesting lack of carcinogenicity: Adequate studies involving at least two species are available which show that, within the limits of the tests used, the agent or mixture is not carcinogenic. A conclusion of evidence suggesting lack of carcinogenicity is inevitably limited to the species, tumour sites and levels of exposure studied.

(*b*) *Other data relevant to the evaluation of carcinogenicity and its mechanisms*

Other evidence judged to be relevant to an evaluation of carcinogenicity and of sufficient importance to affect the overall evaluation is then described. This may include data on preneoplastic lesions, tumour pathology, genetic and related effects, structure-activity relationships, metabolism and pharmacokinetics, physicochemical parameters and analogous biological agents.

Data relevant to mechanisms of the carcinogenic action are also evaluated. The strength of the evidence that any carcinogenic effect observed is due to a particular mechanism is assessed, using terms such as weak, moderate or strong. Then, the Working Group assesses if that particular mechanism is likely to be operative in humans. The strongest indications that a particular mechanism operates in humans come from data on humans or biological specimens obtained from exposed humans. The data may be considered to be especially relevant if they show that the agent in question has caused changes in exposed humans that are on the causal pathway to carcinogenesis. Such data may, however, never become available, because it is at least conceivable that certain compounds may be kept from human use solely on the basis of evidence of their toxicity and/or carcinogenicity in experimental systems.

For complex exposures, including occupational and industrial exposures, the chemical composition and the potential contribution of carcinogens known to be present are considered by the Working Group in its overall evaluation of human carcinogenicity. The Working Group also determines the extent to which the materials tested in experimental systems are related to those to which humans are exposed.

(*c*) *Overall evaluation*

Finally, the body of evidence is considered as a whole, in order to reach an overall evaluation of the

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carcinogenicity to humans of an agent, mixture or circumstance of exposure.

An evaluation may be made for a group of chemical compounds that have been evaluated by the Working Group. In addition, when supporting data indicate that other, related compounds for which there is no direct evidence of capacity to induce cancer in humans or in animals may also be carcinogenic, a statement describing the rationale for this conclusion is added to the evaluation narrative; an additional evaluation may be made for this broader group of compounds if the strength of the evidence warrants it.

The agent, mixture or exposure circumstance is described according to the wording of one of the following categories, and the designated group is given. The categorization of an agent, mixture or exposure circumstance is a matter of scientific judgement, reflecting the strength of the evidence derived from studies in humans and in experimental animals and from other relevant data.

- *Group 1: The agent (mixture) is carcinogenic to humans.*
  The exposure circumstance entails exposures that are carcinogenic to humans.

This category is used when there is *sufficient evidence* of carcinogenicity in humans. Exceptionally, an agent (mixture) may be placed in this category when evidence in humans is less than sufficient but there is *sufficient evidence* of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent (mixture) acts through a relevant mechanism of carcinogenicity.

- *Group 2*

This category includes agents, mixtures and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents, mixtures and exposure circumstances are assigned to either group 2A (probably carcinogenic to humans) or group 2B (possibly carcinogenic to humans) on the basis of epidemiological and experimental evidence of carcinogenicity and other relevant data.

- *Group 2A: The agent (mixture) is probably carcinogenic to humans.*
  The exposure circumstance entails exposures that are probably carcinogenic to humans.

This category is used when there is *limited evidence* of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and *sufficient evidence* of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent, mixture or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.

- *Group 2B: The agent (mixture) is possibly carcinogenic to humans.*
  The exposure circumstance entails exposures that are possibly carcinogenic to humans.

This category is used for agents, mixtures and exposure circumstances for which there is *limited evidence* of carcinogenicity in humans and less than *sufficient evidence* of carcinogenicity in experimental animals. It may also be used when there is *inadequate evidence* of carcinogenicity in humans but there is *sufficient evidence* of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is *inadequate evidence* of carcinogenicity in humans but *limited evidence* of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

- *Group 3: The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.*

This category is used most commonly for agents, mixtures and exposure circumstances for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals.

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Exceptionally, agents (mixtures) for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans.

Agents, mixtures and exposure circumstances that do not fall into any other group are also placed in this category.

- *Group 4: The agent (mixture) is probably not carcinogenic to humans.*

This category is used for agents or mixtures for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents or mixtures for which there is *inadequate evidence* of carcinogenicity in humans but

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PO#:

MATERIAL SAFETY DATA SHEET

- - - - IDENTIFICATION - - - -

PRODUCT #: 21515-5
CAS #:302-01-2 NAME: HYDRAZINE, ANHYDROUS, 98%
MF: H4N2

SYNONYMS
ANHYDROUS HYDRAZINE (UN2029) (DOT) * DIAMIDE * DIAMINE * HYDRAZINE (ACGIH,OSHA) * HYDRAZINE, ANHYDROUS (UN2029) (DOT) * HYDRAZINE, AQUEOUS SOLUTION (UN2030) (DOT) * HYDRAZYNA (POLISH) * RCRA WASTE NUMBER U133 * UN 2029 (DOT) * UN 2030 (DOT) *

- - - - TOXICITY HAZARDS - - - -

RTECS #: MU7175000
HYDRAZINE

TOXICITY DATA

ORL-RAT LD50:60 MG/KG	MEPAAX 24,71,73
IHL-RAT LC50:570 PPM/4H	AMIHAB 12,609,55
IPR-RAT LD50:59 MG/KG	MEPAAX 24,71,73
IVN-RAT LD50:55 MG/KG	MEPAAX 24,71,73
IMS-RAT LD50:53500 UG/KG	GTPZAB 6(6),53,72
ORL-MUS LD50:59 MG/KG	MEPAAX 24,71,73
IHL-MUS LC50:252 PPM/4H	AMIHAB 12,609,55
IPR-MUS LD50:62 MG/KG	MEPAAX 24,71,73
IVN-MUS LD50:57 MG/KG	MEPAAX 24,71,73
UNR-MUS LD50:200 MG/KG	BJCAAI 6,160,52
IVN-DOG LD50:25 MG/KG	MEPAAX 24,71,73
IMS-DOG LD50:16500 UG/KG	GTPZAB 6(6),53,72
SKN-RBT LD50:91 MG/KG	AMIHBC 9,199,54
IVN-RBT LD50:20 MG/KG	AMIHBC 9,199,54
IMS-RBT LD50:38500 UG/KG	GTPZAB 6(6),53,72
SKN-GPG LD50:190 MG/KG	XAWPA2 CHL 2-10,58

REVIEWS, STANDARDS, AND REGULATIONS
ACGIH TLV-SUSPECTED CARCINOGEN 85INAB 5,310(89),86
ACGIH TLV-TWA 0.01 PPM (SKIN) 85INAB 5,310(89),86
IARC CANCER REVIEW:ANIMAL SUFFICIENT EVIDENCE IMEMDT 4,127,74
IARC CANCER REVIEW:HUMAN INADEQUATE EVIDENCE IMSUDL 7,223,87
IARC CANCER REVIEW:GROUP 2B IMSUDL 7,223,87
MSHA STANDARD-AIR:TWA 1 PPM (1.3 MG/M3) (SKIN) OTLVS* 3,127,71
OSHA PEL:8H TWA 1 PPM (1.3 MG/M3)(SKIN) FEREAC 54,2923,89
OSHA PEL FINAL:8H TWA 0.1 PPM (0.1 MG/M3)(SKIN) FEREAC 54,2923,89
OEL-AUSTRALIA:TWA 0.1 PPM (0.1 MG/M3);SKIN;CARCINOGEN JANUARY 1993
OEL-CZECHOSLOVAKIA:TWA 0.05 MG/M3;STEL 0.1 MG/M3 JANUARY 1993

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PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - TOXICITY HAZARDS - - - -

OEL-DENMARK:TWA 0.1 PPM (0.13 MG/M3);SKIN;CARCINOGEN JANUARY 1993
OEL-FINLAND:TWA 0.1 PPM (0.13 MG/M3);STEL 0.3 PPM (0.4 MG/M3);SKIN;
CARCINOGEN JANUARY 1993
OEL-FRANCE:TWA 0.1 PPM (0.1 MG/M3);CARCINOGEN JANUARY 1993
OEL-GERMANY;SKIN;CARCINOGEN JANUARY 1993
OEL-RUSSIA:STEL 0.1 MG/M3;SKIN JANUARY 1993
OEL-SWEDEN:TWA 0.1 PPM (0.1 MG/M3);STEL 0.3 PPM (0.4 MG/M3);SKIN;
CARCINOGEN JANUARY 1993
OEL-SWITZERLAND:TWA 0.1 PPM (0.13 MG/M3);SKIN;CARCINOGEN JANUARY 1993
OEL-THE NETHERLANDS:TWA 0.1 PPM (0.13 MG/M3);SKIN JANUARY 1993
OEL-THE PHILLIPPINES:TWA 1 PPM (1.3 MG/M3);SKIN JANUARY 1993
OEL-TURKEY:TWA 1 PPM (1.3 MG/M3);SKIN JANUARY 1993
OEL-UNITED KINGDOM;SKIN JANUARY 1993
OEL IN BULGARIA, COLOMBIA, JORDAN, KOREA, NEW ZEALAND, SINGAPORE,
VIETNAM CHECK ACGIH TLV
NIOSH REL TO HYDRAZINES-AIR:CA CL 0.03 PPM/120M NIOSH* DHHS #92-100,92
NOHS 1974: HZD 38110; NIS 37; TNF 2134; NOS 27; TNE 11185
NOES 1983: HZD 38110; NIS 44; TNF 2515; NOS 46; TNE 60490; TFE 2841
EPA GENETOX PROGRAM 1988, POSITIVE: CARCINOGENICITY-MOUSE/RAT
EPA GENETOX PROGRAM 1988, INCONCLUSIVE: D MELANOGASTER SEX-LINKED
LETHAL
EPA TSCA CHEMICAL INVENTORY, JUNE 1990
ON EPA IRIS DATABASE
EPA TSCA TEST SUBMISSION (TSCATS) DATA BASE, JANUARY 1993
NIOSH ANALYTICAL METHODS: SEE HYDRAZINE, 3503
NTP 7TH ANNUAL REPORT ON CARCINOGENS, 1992 : ANTICIPATED TO BE
CARCINOGEN
OSHA ANALYTICAL METHOD #20

TARGET ORGAN DATA
SENSE ORGANS AND SPECIAL SENSES (OLFACTION TUMORS)
SENSE ORGANS AND SPECIAL SENSES (OTHER EYE EFFECTS)
BEHAVIORAL (CONVULSIONS OR EFFECT ON SEIZURE THRESHOLD)
LUNGS, THORAX OR RESPIRATION (DYSPNAE)
LUNGS, THORAX OR RESPIRATION (TUMORS)
GASTROINTESTINAL (COLON TUMORS)
LIVER (TUMORS)
ENDOCRINE (THYROID TUMORS)
BLOOD (TUMORS)

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CUST#: 413003

PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - TOXICITY HAZARDS - - - -

BLOOD (LEUKEMIA)
BLOOD (LYMPHOMA INCLUDING HODGKIN'S DISEASE)
PATERNAL EFFECTS (TESTES, EPIDIDYMIS, SPERM DUCT)
MATERNAL EFFECTS (OVARIES, FALLOPIAN TUBES)
EFFECTS ON FERTILITY (POST-IMPLANTATION MORTALITY)
EFFECTS ON EMBRYO OR FETUS (FETOTOXICITY)
EFFECTS ON EMBRYO OR FETUS (FETAL DEATH)
SPECIFIC DEVELOPMENTAL ABNORMALITIES (CENTRAL NERVOUS SYSTEM)
SPECIFIC DEVELOPMENTAL ABNORMALITIES (MUSCULOSKELETAL SYSTEM)
SPECIFIC DEVELOPMENTAL ABNORMALITIES (UROGENITAL SYSTEM)
EFFECTS ON NEWBORN (VIABILITY INDEX)
TUMORIGENIC (CARCINOGENIC BY RTECS CRITERIA)
TUMORIGENIC (NEOPLASTIC BY RTECS CRITERIA)
TUMORIGENIC (EQUIVOCAL TUMORIGENIC AGENT BY RTECS CRITERIA)
ONLY SELECTED REGISTRY OF TOXIC EFFECTS OF CHEMICAL SUBSTANCES (RTECS) DATA IS PRESENTED HERE. SEE ACTUAL ENTRY IN RTECS FOR COMPLETE INFORMATION.

- - - - HEALTH HAZARD DATA - - - -

ACUTE EFFECTS

MAY BE FATAL IF INHALED, SWALLOWED, OR ABSORBED THROUGH SKIN.
MATERIAL IS EXTREMELY DESTRUCTIVE TO TISSUE OF THE MUCOUS MEMBRANES AND UPPER RESPIRATORY TRACT, EYES AND SKIN.
INHALATION MAY BE FATAL AS A RESULT OF SPASM, INFLAMMATION AND EDEMA OF THE LARYNX AND BRONCHI, CHEMICAL PNEUMONITIS AND PULMONARY EDEMA.
SYMPTOMS OF EXPOSURE MAY INCLUDE BURNING SENSATION, COUGHING, WHEEZING, LARYNGITIS, SHORTNESS OF BREATH, HEADACHE, NAUSEA AND VOMITING.
MAY CAUSE ALLERGIC REACTION.
CAN CAUSE CNS DEPRESSION.
MAY CAUSE CONVULSIONS.
EXPOSURE CAN CAUSE:
DAMAGE TO THE EYES
DAMAGE TO THE LIVER
DAMAGE TO THE KIDNEYS
DAMAGE TO THE LUNGS
BLOOD EFFECTS

CHRONIC EFFECTS

CARCINOGEN.

CONTINUED ON NEXT PAGE

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CUST#: 413003

PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - HEALTH HAZARD DATA - - - -

MAY ALTER GENETIC MATERIAL.
TARGET ORGAN(S):
NERVES
BLOOD
LIVER, KIDNEYS

FIRST AID
IN CASE OF CONTACT, IMMEDIATELY FLUSH EYES OR SKIN WITH COPIOUS AMOUNTS OF WATER FOR AT LEAST 15 MINUTES WHILE REMOVING CONTAMINATED CLOTHING AND SHOES.
ASSURE ADEQUATE FLUSHING OF THE EYES BY SEPARATING THE EYELIDS WITH FINGERS.
IF INHALED, REMOVE TO FRESH AIR. IF NOT BREATHING GIVE ARTIFICIAL RESPIRATION. IF BREATHING IS DIFFICULT, GIVE OXYGEN.
IF SWALLOWED, WASH OUT MOUTH WITH WATER PROVIDED PERSON IS CONSCIOUS.
CALL A PHYSICIAN.
DISCARD CONTAMINATED CLOTHING AND SHOES.

- - - - PHYSICAL DATA - - - -

BOILING POINT: 113.5 C
MELTING POINT: 1.4 C
SPECIFIC GRAVITY: 1.021
VAPOR DENSITY: 1 @ 37 C
VAPOR PRESSURE: 10 MM @ 30.7 C

APPEARANCE AND ODOR
CLEAR COLORLESS LIQUID

- - - - FIRE AND EXPLOSION HAZARD DATA - - - -

FLASHPOINT 126 F
LOWER EXPLOSION LEVEL: 4.7%
UPPER EXPLOSION LEVEL: 99.99%

EXTINGUISHING MEDIA
WATER SPRAY.
CARBON DIOXIDE.
DRY CHEMICAL POWDER.

CONTINUED ON NEXT PAGE

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CUST#: 413003

PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - FIRE AND EXPLOSION HAZARD DATA - - - -

SPECIAL FIREFIGHTING PROCEDURES
WEAR SELF-CONTAINED BREATHING APPARATUS AND PROTECTIVE CLOTHING TO PREVENT CONTACT WITH SKIN AND EYES.
COMBUSTIBLE LIQUID.

UNUSUAL FIRE AND EXPLOSIONS HAZARDS
CATCHES FIRE IF EXPOSED TO AIR.
MAY EXPLODE WHEN HEATED.
REDUCING AGENT.
EMITS TOXIC FUMES UNDER FIRE CONDITIONS.

- - - - REACTIVITY DATA - - - -

INCOMPATIBILITIES
OXIDIZING AGENTS
OXYGEN
COPPER
IRON
ORGANIC MATERIALS

HAZARDOUS COMBUSTION OR DECOMPOSITION PRODUCTS
NITROGEN OXIDES

- - - - SPILL OR LEAK PROCEDURES - - - -

STEPS TO BE TAKEN IF MATERIAL IS RELEASED OR SPILLED
EVACUATE AREA.
WEAR SELF-CONTAINED BREATHING APPARATUS, RUBBER BOOTS AND HEAVY RUBBER GLOVES.
ABSORB ON SAND OR VERMICULITE AND PLACE IN CLOSED CONTAINERS FOR DISPOSAL.
VENTILATE AREA AND WASH SPILL SITE AFTER MATERIAL PICKUP IS COMPLETE.

WASTE DISPOSAL METHOD
THIS COMBUSTIBLE MATERIAL MAY BE BURNED IN A CHEMICAL INCINERATOR EQUIPPED WITH AN AFTERBURNER AND SCRUBBER.
OBSERVE ALL FEDERAL, STATE AND LOCAL ENVIRONMENTAL REGULATIONS.

- - - - PRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE - - - -

WEAR APPROPRIATE NIOSH/MSHA-APPROVED RESPIRATOR, CHEMICAL-RESISTANT GLOVES, SAFETY GOGGLES, OTHER PROTECTIVE CLOTHING.

CONTINUED ON NEXT PAGE

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PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - PRECAUTIONS TO BE TAKEN IN HANDLING AND STORAGE - - - -

USE ONLY IN A CHEMICAL FUME HOOD.
SAFETY SHOWER AND EYE BATH.
FACESHIELD (8-INCH MINIMUM).
DO NOT BREATHE VAPOR.
DO NOT GET IN EYES, ON SKIN, ON CLOTHING.
AVOID PROLONGED OR REPEATED EXPOSURE.
READILY ABSORBED THROUGH SKIN.
WASH THOROUGHLY AFTER HANDLING.
HIGHLY TOXIC.
CORROSIVE.
SENSITIZER.
CARCINOGEN.
MUTAGEN.
KEEP TIGHTLY CLOSED.
KEEP AWAY FROM HEAT AND OPEN FLAME.
STORE IN A COOL DRY PLACE.

LABEL PRECAUTIONARY STATEMENTS
COMBUSTIBLE (USA DEFINITION)
FLAMMABLE (EUROPEAN DEFINITION)
HIGHLY TOXIC (USA DEFINITION)
TOXIC (EUROPEAN DEFINITION)
MAY CAUSE CANCER.
MAY CAUSE HERITABLE GENETIC DAMAGE.
TOXIC BY INHALATION, IN CONTACT WITH SKIN AND IF SWALLOWED.
CAUSES BURNS.
COMBUSTIBLE LIQUID.
SENSITIZER.
TARGET ORGAN(S):
LIVER
BLOOD
KEEP AWAY FROM SOURCES OF IGNITION. NO SMOKING.
IF YOU FEEL UNWELL, SEEK MEDICAL ADVICE (SHOW THE LABEL WHERE POSSIBLE).
IN CASE OF CONTACT WITH EYES, RINSE IMMEDIATELY WITH PLENTY OF WATER AND SEEK MEDICAL ADVICE.
WEAR SUITABLE PROTECTIVE CLOTHING, GLOVES AND EYE/FACE PROTECTION.

REGULATORY INFORMATION
THIS PRODUCT IS SUBJECT TO SARA SECTION 313 REPORTING REQUIREMENTS.

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CUST#: 413003

PRODUCT #:

NAME: HYDRAZINE, ANHYDROUS, 98%

MF: H4N2

- - - - ADDITIONAL PRECAUTIONS AND COMMENTS - - - -

ADDITIONAL INFORMATION
WARNING: HYDRAZINE VAPOR IN AIR IS FLAMMABLE AT 4.7 TO 100% HYDRAZINE BY VOLUME - HANDLE UNDER NITROGEN! SOME METALS AND ALLOYS INCLUDING MONEL, BRONZE, BRASS, CADMIUM, GOLD, MOLYBDENUM AND STAINLESS STEEL WITH MORE THAN 0.5% MOLYBDENUM OR RUST CAUSE DECOMPOSITION OF HYDRAZINE.

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Olin

MATERIAL SAFETY DATA

OCEAN NETWORK EMERGENCY PHONE 1-800-OLIN 911

THIS MATERIAL SAFETY DATA SHEET (MSDS) HAS BEEN PREPARED IN COMPLIANCE WITH THE FEDERAL OSHA HAZARD COMMUNICATION STANDARD,29 CFR 1910.1200.THIS PRODUCT MAY BE CONSIDERED TO BE A HAZARDOUS CHEMICAL UNDER THAT STANDARD.(REFER TO THE OSHA CLASSIFICATION IN SEC.I.)THIS INFORMATION IS REQUIRED TO BE DISCLOSED FOR SAFETY IN THE WORKPLACE.THE EXPOSURE TO THE COMMUNITY,IF ANY,IS QUITE DIFFERENT.

I. PRODUCT IDENTIFICATION

REVISION NO : 1
REVISION DATE : 2/18/98
PRODUCT CODE : CPE00567#
FILE NUMBER : CPE00338.0003
PRODUCT NAME: UNSYMMETRICAL DIMETHYLHYDRAZINE
SYNONYMS: 1,1-Dimethylhydrazine, UDMH
CHEMICAL FAMILY: Hydrazine
FORMULA: $C_2H_8N_2$
USE DESCRIPTION: Propellant
OSHA HAZARD CLASSIFICATION: Carcinogen; corrosive; toxic by ingestion and inhalation; sensitizer; liver, kidney, nervous system, blood, and lung toxin; skin and eye hazard; flammable

II. COMPONENT DATA

PRODUCT COMPOSITION:
CAS or CHEMICAL NAME: 1,1-dimethylhydrazine
CAS NUMBER: 57-14-7
PERCENTAGE RANGE: 95-99
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:	0.5	1 (skin)	0.01	0.025 (skin)
CEILING:	None		None	
STEL:	None		None	

OC 932

BNA08768261

HDMSP001793948

CAS or CHEMICAL NAME: Dimethyl amine
CAS NUMBER: 124-40-3
PERCENTAGE RANGE: 1-5
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:	10	18	5	9.2
CEILING:	None		None	
STEL:	None		15	27.6

CAS or CHEMICAL NAME: Water
CAS NUMBER: 7732-18-5
PERCENTAGE RANGE: 0.1-1
HAZARDOUS PER 29 CFR 1910.1200: No
EXPOSURE STANDARDS: None Established

III. PRECAUTIONS FOR SAFE HANDLING AND STORAGE

DO NOT TAKE INTERNALLY. AVOID CONTACT WITH SKIN, EYES AND CLOTHING. UPON CONTACT WITH SKIN OR EYES, WASH OFF WITH WATER. AVOID BREATHING MIST OR VAPOR.

STORAGE CONDITIONS: Store away from heat, sparks, open flame and oxidants. Store only in well-ventilated areas. Do not contaminate. All containers and handling equipment for 1,1-dimethyl hydrazine should be electrically grounded. An inert atmosphere must be maintained over 1,1-dimethyl hydrazine at all times. Nitrogen has been adopted as the padding material for 1,1-dimethyl hydrazine storage and transfer.
DO NOT STORE AT TEMPERATURES ABOVE: 51 Deg.C (124 Deg.F)
OTHER: DO NOT EXPOSE TO DIRECT LIGHT.

PRODUCT STABILITY AND COMPATIBILITY

SHELF LIFE LIMITATIONS: 5 Years if not opened and exposed to the atmosphere. Material older than 5 years should be retested before use.

INCOMPATIBLE MATERIALS FOR PACKAGING: Avoid molybdenum-containing alloys such as Hastelloy C and copper-containing alloys. 1,1-Dimethyl hydrazine can be packaged in stainless steels, aluminum, TEFLON(R), and polyethylene.

INCOMPATIBLE MATERIALS FOR STORAGE OR TRANSPORT: Oxidizing agents, metal oxides, and organic materials with high surface area or porous surfaces such as rags, cotton waste, and sawdust

IV. PHYSICAL DATA

APPEARANCE: Clear, colorless liquid
FREEZING POINT: -57 Deg.C (-71 Deg.F)
BOILING POINT: 63 Deg.C (146 Deg.F)
DECOMPOSITION TEMPERATURE: 371 Deg.C (700 Deg.F)

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SPECIFIC GRAVITY: 0.78
BULK DENSITY: 0.784 (g/cc)
pH @ 25 DEG.C: 9.5-10.5 (5% in neutral distilled water)
VAPOR PRESSURE @ 25 DEG.C: 157 mm Hg
SOLUBILITY IN WATER: Completely miscible
VOLATILES, PERCENT BY VOLUME: 100
EVAPORATION RATE: No Data
VAPOR DENSITY: 2.1 (air=1)
MOLECULAR WEIGHT: 60.10
ODOR: Ammonia
COEFFICIENT OF OIL/WATER DISTRIBUTION: No Data

V. PERSONAL PROTECTIVE EQUIPMENT REQUIREMENTS

PERSONAL PROTECTION FOR ROUTINE USE OF PRODUCT:

RESPIRATORY PROTECTION: Wear a NIOSH/MSHA approved respirator if any exposure occurs.

VENTILATION: Use explosion-proof local exhaust ventilation to maintain levels to below the TLV.

SKIN AND EYE PROTECTIVE EQUIPMENT: Wear gloves, boots, apron and a face shield with safety glasses. A full impermeable suit is recommended if exposure is possible to large portion of body.

OTHER: Eye wash and safety shower must be immediately available where material is handled.

EQUIPMENT SPECIFICATIONS (WHEN APPLICABLE):

RESPIRATOR TYPE:	NIOSH/MSHA approved full-face positive-pressure supplied air respirator
GLOVE TYPE:	Butyl rubber
BOOT TYPE:	Butyl rubber
APRON TYPE:	Butyl rubber
PROTECTIVE SUIT:	Butyl rubber

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VI. FIRE AND EXPLOSION HAZARD INFORMATION

FLAMMABILITY DATA:
- FLAMMABLE: Yes
- COMBUSTIBLE: Not Applicable
- PYROPHORIC: No
- FLASH POINT: -15 Deg.C (5 Deg.F) Test Method: Cleveland open cup
- AUTOIGNITION TEMPERATURE: 250 Deg.C (482 Deg.F)
- FLAMMABLE LIMITS AT NORMAL ATMOSPHERIC TEMPERATURE AND PRESSURE (PERCENT VOLUME IN AIR): LEL - 2% UEL - 95%

NFPA RATINGS:
- HEALTH: 4
- FLAMMABILITY: 3
- REACTIVITY: 1

HMIS RATINGS:
- HEALTH: 3
- FLAMMABILITY: 3
- REACTIVITY: 1

EXTINGUISHING MEDIA: Carbon dioxide, dry chemical, water spray
FIRE FIGHTING TECHNIQUES AND COMMENTS: Use water to cool containers exposed to fire. See section XI for protective equipment for fire fighting.

VII. REACTIVITY INFORMATION

CONDITIONS UNDER WHICH THIS PRODUCT MAY BE UNSTABLE:
- TEMPERATURES ABOVE: 250 Deg.C (482 Deg.F)
- MECHANICAL SHOCK OR IMPACT: No
- ELECTRICAL (STATIC) DISCHARGE: Yes
- HAZARDOUS POLYMERIZATION: Will not occur
- INCOMPATIBLE MATERIALS: Avoid contact between 1,1-dimethyl hydrazine and strong oxidizers such as hydrogen peroxide, nitrogen tetroxide, fluorine, halogen fluorides, and fuming nitric acid. Such contact will result in immediate ignition or explosion. Avoid contact with metal oxides such as those of iron, copper, lead, manganese, and molybdenum. Contact with such metallic oxide surfaces may lead to flaming decomposition. Avoid contact with organic materials having large surface areas or porous surfaces. Adsorption of 1,1-dimethyl hydrazine by rags, cotton waste, sawdust or similar organic materials will eventually result in spontaneous ignition.
- HAZARDOUS DECOMPOSITION PRODUCTS: Carbon monoxide, nitrogen oxides

SUMMARY OF REACTIVITY:
- OXIDIZER: No
- PYROPHORIC: No
- ORGANIC PEROXIDE: No
- WATER REACTIVE: No

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VIII. FIRST AID

EYES: Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Call a physician at once.

SKIN: Immediately flush with water for at least 15 minutes. Call a physician. If clothing comes in contact with the product, the clothing should be removed immediately and should be laundered before re-use.

INGESTION: Immediately drink large quantities of water. Induce vomiting. Call a physician at once. DO NOT give anything by mouth if the person is unconscious or if having convulsions.

INHALATION: If person experiences nausea, headache or dizziness, person should stop work immediately and move to fresh air until these symptoms disappear. If breathing is difficult, administer oxygen, keep the person warm and at rest. Call a physician. In the event that an individual inhales enough vapor to lose consciousness, person should be moved to fresh air at once and a physician should be called immediately. If breathing has stopped, artificial respiration should be given immediately. In all cases, ensure adequate ventilation and provide respiratory protection before the person returns to work.

IX. TOXICOLOGY AND HEALTH INFORMATION

ROUTES OF ABSORPTION
Inhalation, dermal, oral, eye contact

WARNING STATEMENTS AND WARNING PROPERTIES
HARMFUL IF INHALED OR SWALLOWED. MAY BE HARMFUL IF ABSORBED THROUGH SKIN. CAUSES EYE, SKIN, DIGESTIVE TRACT AND RESPIRATORY TRACT BURNS. CAUSES LIVER, LUNG, KIDNEY, BLOOD, AND NERVOUS SYSTEM DAMAGE. MAY CAUSE AN ALLERGIC SKIN REACTION. MAY CAUSE CANCER BASED ON ANIMAL DATA.

HUMAN THRESHOLD RESPONSE DATA
ODOR THRESHOLD: 6-14 ppm
IRRITATION THRESHOLD: This value has not been established.
IMMEDIATELY DANGEROUS TO LIFE OR HEALTH: 15 ppm

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SIGNS, SYMPTOMS, AND EFFECTS OF EXPOSURE

INHALATION

ACUTE:

Highly irritating to the nose, throat, upper respiratory tract and lungs. Inflammation of the respiratory tract may lead to bronchitis. Pulmonary edema and lung damage may occur. Toxic if inhaled and rapidly absorbed through the lungs. Damage may also result to liver, kidneys and blood. High exposure may give rise to hemolysis of the blood cells. Vomiting, diarrhea, nausea, dizziness, hypoglycemia, cyanosis and convulsions may also occur.

CHRONIC:

Repeated inhalation may produce inflammation of the nasal, tracheal and bronchial tissue. Chronic bronchitis can result. Damage to the liver, kidneys, and blood may also occur. Damage to blood may be characterized by hemolysis and reduction of packed cell volume. Repeated inhalation of 1,1-dimethylhydrazine has produced cancer in laboratory animals.

SKIN

ACUTE:

1,1-dimethylhydrazine is rapidly absorbed through the skin and is highly toxic by this route which is dependant on exposed skin surface and concentration of the solution. Exposure to large areas of the skin may lead to a significant dose being absorbed causing systemic toxicity similar to the effects described for inhalation exposure. Additionally, 1,1-dimethylhydrazine can produce severe irritation and/or burns. Dermatitis may also occur.

CHRONIC:

Repeated exposure can cause an allergic reaction resulting in dermatitis and a characteristic rash. Other effects would be similar to those described under chronic inhalation.

EYE

Exposure can cause inflammation, swelling, redness, and discharge. Temporary blindness can occur. If not rinsed immediately from the eyes, burns and permanent corneal damage can occur resulting in impairment of vision.

INGESTION

ACUTE:

Irritation and/or burns can occur to the entire gastrointestinal tract, including the stomach and intestines, characterized by nausea, vomiting, diarrhea, abdominal pain, bleeding, and/or tissue ulceration. Toxic by ingestion causing effects similar to those as stated under inhalation exposure.

CHRONIC:

Inflammation to the gastrointestinal tract can occur. Other effects would be similar as stated under inhalation exposure. Repeated ingestion of has produced cancer in laboratory animals.

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MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE
Diseases of the liver, kidneys, and blood, as well as asthma and cardiovascular disease and nervous system disorders.

INTERACTIONS WITH OTHER CHEMICALS WHICH ENHANCE TOXICITY:
None known or reported

ANIMAL TOXICOLOGY
ACUTE TOXICITY:
Inhalation LC 50: Approximately 252 ppm (4 hrs. exposure, rats)
Dermal LD 50: 1.05 g/kg. (rabbit)
Oral LD 50: 122 mg/kg. (rats)
Irritation: Corrosive to skin and eyes; respiratory irritant

ACUTE TARGET ORGAN TOXICITY:
Damage to lungs, liver, kidneys, blood and central nervous system.

CHRONIC TARGET ORGAN TOXICITY:
Repeated exposure to 1,1-dimethylhydrazine and dimethylamine has produced damage to the lungs, liver, kidneys, blood and nervous system. Cancer has also been observed in laboratory animals from exposure to 1,1-dimethylhydrazine.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY:
High concentrations of 1,1-dimethylhydrazine have produced embryolethality and fetal malformations to the offspring of animals exposed during pregnancy. These findings were only osbserved at concentrations that cause significant maternal toxicity. Under industrial use conditions where exposures are kept at or below the recommended occupational exposure standards, exposure to this product should not pose a reproductive and developmental toxicity hazard.

CARCINOGENICITY:
1,1-Dimethylhydrazine is recognized as a cancer-causing agent in animals by IARC and OSHA. It is considered to be a suspect carcinogen in humans by these two organizations.

MUTAGENICITY:
1,1-Dimethylhydrazine has been shown to cause DNA and chromosomal damage in a number of test systems. It is considered mutagenic.

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AQUATIC TOXICITY:
No available data

X. TRANSPORTATION INFORMATION

THIS MATERIAL IS REGULATED AS A DOT HAZARDOUS MATERIAL.

DOT DESCRIPTION FROM THE HAZARDOUS MATERIALS TABLE 49 CFR 172.101:
LAND (U.S. DOT): DIMETHYLHYDRAZINE, UNSYMMETRICAL, 6.1, UN1163, PG I, Poison Inhalation Hazard - Hazard Zone B

WATER (IMO): SAME AS ABOVE

AIR (IATA/ICAO): FORBIDDEN

HAZARD LABEL/PLACARD: TOXIC
FLAMMABLE LIQUID
CORROSIVE
REPORTABLE QUANTITY: 10 lbs. (Per 49 CFR 172.101, Appendix)
EMERGENCY GUIDE NUMBER: 131

XI. SPILL AND LEAKAGE PROCEDURES

FOR ALL TRANSPORTATION ACCIDENTS, CALL CHEMTREC AT 800-424-9300.

REPORTABLE QUANTITY: This product is subject to a Reportable Quantity with respect to dimethylhydrazine. RQs are subject to change and reference should be made to 40 CFR 302.4 for the current requirements

SPILL MITIGATION PROCEDURES:
Evacuation procedures must be placed into effect. Hazardous concentrations in air may be found in local spill area and immediately downwind. This product may represent an explosion hazard. Remove all sources of ignition. Stop source of spill as soon as possible and notify appropriate personnel.

AIR RELEASE: Vapors may be suppressed by the use of water fog. Contain all liquid for treatment or neutralization.

WATER RELEASE: This material is lighter than and soluble in water. Notify all downstream water users of possible contamination. Divert water flow around spill if possible and safe to do so. Remove with a vacuum system or pumping device for treatment and/or disposal. Continue to handle as described in land spill.

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LAND SPILL: Dike spill area immediately. Dilute material to bring the concentration of UDMH to below 30% or 2 1/2 to 1 water to UDMH. Remove as a liquid and containerize for proper disposal or other use. Always place material in container appropriate for this product as described in Section III. Label according to local, state, and federal regulations. Decontaminate spill area by diluting further with water to a 5% or less solution. Add an equal volume of 5% calcium hypochlorite aqueous solution. Test for neutralization. After neutralization, scrub with a strong detergent and rinse with large volumes of water. Wash all clothing as soon as possible. Do not allow to dry completely. Discard any contaminated leather articles.

SPILL RESIDUES:
Dispose of per guidelines under Section XII, WASTE DISPOSAL.

This material may be neutralized for disposal; you are requested to contact OCEAN at 800-OLIN-911 before beginning any such operation.

PERSONAL PROTECTION FOR EMERGENCY SPILL AND FIRE-FIGHTING SITUATIONS:
In case of fire, use normal fire fighting equipment.

Additional respiratory protection is necessary when a spill or fire involving this product occurs. You are recommended to use a self-contained breathing apparatus (SCBA) positive pressure unit.

Additional protective clothing must be worn to prevent personal contact with this material. Those items include but are not limited to boots, gloves, hard hat, splash-proof goggles, full face shield and impervious clothing, i.e., chemically impermeable or fully encapsulated suit. Compatible material for response to this material is butyl rubber.

Protection concerns must also address the potential of the physical characteristics of this product as poison by inhalation.

XII. WASTE DISPOSAL

If this product becomes a waste, it meets the criteria of a hazardous waste as defined under 40 CFR 261 and would have the following EPA hazardous waste number: D001, U098.

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If this product becomes a waste, it will be a hazardous waste which is subject to the Land Disposal Restrictions under 40 CFR 268 and must be managed accordingly.

As a hazardous liquid waste, it must be disposed of in accordance with local, state and federal regulations in a permitted hazardous waste treat ment, storage and disposal facility by incineration.

CARE MUST BE TAKEN TO PREVENT ENVIRONMENTAL CONTAMINATION FROM THE USE OF THIS MATERIAL. THE USER OF THIS MATERIAL HAS THE RESPONSIBILITY TO DISPOSE OF UNUSED MATERIAL, RESIDUES AND CONTAINERS IN COMPLIANCE WITH ALL RELEVANT LOCAL, STATE AND FEDERAL LAWS AND REGULATIONS REGARDING TREATMENT, STORAGE AND DISPOSAL FOR HAZARDOUS AND NONHAZARDOUS WASTES.

XIII. ADDITIONAL REGULATORY STATUS INFORMATION

TOXIC SUBSTANCES CONTROL ACT:
The components of this product are listed on the Toxic Substance Control Act inventory.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 - PROPOSITION 65:
"WARNING: This product contains detectable amounts of a chemical known to the State of California to cause cancer and birth defects or other reproductive harm."

SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT TITLE III:
HAZARD CATEGORIES, PER 40 CFR 370.2:
HEALTH:
Immediate (Acute)
Delayed (Chronic)
PHYSICAL:
Fire

EMERGENCY PLANNING AND COMMUNITY RIGHT TO KNOW, PER 40 CFR 355, APP. A:
EXTREMELY HAZARDOUS SUBSTANCES - THRESHOLD PLANNING QUANTITY:
1,000 lbs. (Dimethylhydrazine)
SUPPLIER NOTIFICATION REQUIREMENTS, PER 40 CFR 372.45:
This mixture or tradename product contains a toxic chemical or chemicals subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40 CFR 372.
Chemicals listed are: 1,1-Dimethylhydrazine, dimethyl amine

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XIV. ADDITIONAL INFORMATION

MSDS REVISION STATUS: Emergency guide number revised in Section X. (09)

XV. MAJOR REFERENCES

1. Haun, C. C., et al. October 1984. Chronic Inhalation Toxicity of Unsymmetrical Dimethylhydrazine: Oncogenic Effects. Air Force Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio AFAMRL-TR-85-020.
2. Litton Bionetics, Inc.,. December 1976. Mutagen and Oncogen Study on 1,1-Dimethylhydrazine Final Report. Air Force Systems Command, Wright-Patterson Air Force Base, Ohio. AMRL-TR-76-78.
3. Rinehart, W.E., et al. June 1960. The Sub-Acute and Chronic Toxicity of 1,1-Dimethylhydrazine Vapor. Army Chemical Center, Maryland.
4. Toth, B. 1,1-Dimethylhydrazine (Unsymmetrical) Carcinogenesis in Mice. Light Microscopic and Ultrastructural Studies on Neoplastic Blood Vessels. University of Nebraska College of Medicine, Omaha, Nebraska.
5. Cornish, H. H., Hartung, R. 1969. The Subacute Toxicity of 1,1-Dimethylhydrazine. The University of Michigan, Ann Arbor, Michigan. Toxicology and Applied Pharmacology 15, 62-68.
6. Keller, W. C., et al. 1984. Teratogenic Assessment of Three Methylated Hydrazine Derivatives in the Rat. Hazards Division, Wright-Patterson AFB, Ohio. Journal of Toxicology and Environmental Health, 13:125-131.
7. Reinhardt, C. F. et al. 1965. Toxicity of Hydrazine and 1,1-Dimethyl-hydrazine (UDMH). Columbus, Ohio. Arch Environ Health Vol. 10.
8. Kimball, R. F. 1977. The Mutagenicity of Hydrazine and Some of its Derivatives. Biology Division, Oak Ridge National Laboratory, Tennessee.

Other References are available upon request.

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THE INFORMATION IN THIS MATERIAL SAFETY DATA SHEET SHOULD BE PROVIDED TO ALL WHO WILL USE, HANDLE, STORE, TRANSPORT, OR OTHERWISE BE EXPOSED TO THIS PRODUCT. THIS INFORMATION HAS BEEN PREPARED FOR THE GUIDANCE OF PLANT ENGINEERING, OPERATIONS AND MANAGEMENT AND FOR PERSONS WORKING WITH OR HANDLING THIS PRODUCT. OLIN BELIEVES THIS INFORMATION TO BE RELIABLE AND UP TO DATE AS OF THE DATE OF PUBLICATION, BUT MAKES NO WARRANTY THAT IT IS. ADDITIONALLY, IF THIS MATERIAL SAFETY DATA SHEET IS MORE THAN THREE YEARS OLD, YOU SHOULD CONTACT OLIN AT THE PHONE NUMBER LISTED BELOW TO MAKE CERTAIN THAT THIS SHEET IS CURRENT.

OLIN MSDS CONTROL GROUP
Olin Corporation
501 Merritt 7
P.O. Box 4500
Norwalk, CT 06856-4500
Phone Number: (800) 511-MSDS

OLIN CORPORATION SUBSIDIARIES AND AFFILIATED ENTITIES: ASAHI-OLIN LTD., BRIDGEPORT BRASS CORPORATION, OLIN AEROSPACE COMPANY, A.J. OSTER COMPANY, OLIN FABRICATED METAL PRODUCTS,INC., OLIN HUNT SPECIALTY PRODUCTS,INC., OLIN SPECIALTY METALS CORPORATION, GENERAL DEFENSE CORPORATION, NIACHLOR, PHYSICS INTERNATIONAL COMPANY, SUPERIOR POOL PRODUCTS, INC., ETOXYL, C.A., OCG MICROELECTRONIC MATERIALS, INC., OLIN ENGINEERED SYSTEMS, INC., YAMAHA-OLIN METAL CORPORATION, NORDESCLOR, S.A.

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EXPLANATION OF THE MATERIAL SAFETY DATA SHEET

The information in the Material Safety Data Sheet (MSDS) is organized into fifteen sections which are as follows:

I Product Identification
II Component Data
III Precautions for Safe Handling and Storage
IV Physical Data
V Personal Protective Equipment Requirements
VI Fire and Explosion Hazard Information
VII Reactivity Information
VIII First Aid
IX Toxicology and Health Information
X Transportation Information
XI Spill and Leak Procedures
XII Waste Disposal
XIII Additional Regulatory Status Information
XIV Additional Information
XV Major References

Section I — *Product Identification*

The product name and product code are used to identify the product. The file number and revision number identify the Material Safety Data Sheet (MSDS) itself. The chemical family or name and synonyms are given with formula where applicable. A brief use description of the product is presented along with the OSHA Hazard Classifications.

Section II — *Component Data*

All Olin products are evaluated to determine if they are hazardous. According to the Occupational Safety and Health Administration (OSHA), a hazardous chemical refers to any chemical that presents a physical hazard or a health hazard. A chemical may be a physical hazard if it is combustible, flammable, pyrophoric, chemically unstable, water reactive or explosive, a compressed gas, an organic peroxide or other oxidizer.

A chemical may present a health hazard if exposure could result in acute or chronic adverse health effects. This definition of a hazardous material has been adapted from the OSHA Hazardous Communication Standard (29 CFR 1910.1200). The reader should refer to the Standard for further details. If it has been determined that a product is not hazardous, then this is stated. If it has been determined that the product is a health hazard then all components that present a health hazard and that comprise 1% or more of the material are listed in this section. Also, any component that is a carcinogen is listed if it comprises 0.1% or more of the product. If it has been determined that the product is a physical hazard, then any component that presents a physical hazard is listed.

Normally, the chemical name and Chemical Abstracts Service (CAS) Number are used to identify a component. CAS numbers are assigned to chemicals and mixtures by the Chemical Abstracts Service (published by the American Chemical Society) as a specific identification. Where the identity of a component is a trade secret, a descriptive name is used instead of the chemical name and a trade secret access number is given to that component. Disclosure of the identity of the trade secret component will be made to health professionals upon request, subject to the conditions specified in the Standard.

Exposure limits are given for each component where these have been established. Definitions of these exposure limits follow:

- **ACGIH TLV (Threshold Limit Value):** A term used by the American Conference of Governmental Industrial Hygienists to express the airborne concentration of a material to which nearly all persons can be exposed day after day without adverse effects. ACGIH expresses TLVs in three ways:
  - **TLV-TWA:** = The allowable Time Weighted Average concentration for a normal 8-hour workday of a 40-hour workweek.
  - **TLV-STEL:** = The Short-Term Exposure Limit, or maximum concentration for a continuous 15-minute exposure period. A maximum of four such periods per day, with at least 60 minutes between exposure periods are allowed, provided that the daily TLV is not exceeded.
  - **TLV-C:** The Ceiling exposure limit; the concentration that should not be exceeded even instantaneously.
  - **SKIN:** A notation used to indicate that the stated substance may be absorbed by the skin, mucous membranes and eyes, either by air or direct contact, and that this additional exposure must be considered part of the total exposure to avoid exceeding TLV for that substance.

  The value quoted is the TWA unless another category is stated.
- **OSHA PEL (Permissible Exposure Limits):** An exposure limit established by the Occupational Safety and Health Administration. May be a time weighted average (TWA) limit or ceiling (C) exposure limit. A skin notation has the same meaning as for the TLV.

Section III — *Precautions for Safe Handling and Storage*

This section provides vital information for handling and storing a product. It is important that all recommendations be followed.

Section IV — *Physical Data*

Knowledge of the physical properties of a substance is necessary for all safety and industrial hygiene decisions. Definitions of terms that apply to the physical data presented in this section are given below:

- **Freezing Point/Melting Point:** The temperature at which a substance changes state from liquid to solid or solid to liquid. For mixtures, a range may be given.
- **Boiling Point:** The temperature at which a liquid changes to a vapor state at a given pressure. (Usually 760 mmHg, or one atmosphere.) For mixtures, the initial boiling point or the boiling range may be given. Flammable materials with low boiling points generally present special fire hazards.
- **Decomposition Temp:** The temperature at which a substance will break down, or decompose, into smaller fragments.
- **Specific Gravity:** The weight of a material compared to

— **LD_{50} (Lethal Dose Fifty)** — The dose of a substance expected to cause the death of 50% of an experimental animal population. This dose may be from oral, dermal or other routes of exposure. The units given for the LD_{50} are usually milligrams per kilogram body weight of the tested animal (mg/kg).

— **LC_{50} (Lethal Concentration Fifty)** — A calculated concentration of a substance in air, exposure to which for a specified length of time is expected to cause the death of 50% of a laboratory animal population. This concentration is usually in units of milligrams per cubic meter of air (mg/m^3) or milligrams per liter of air (mg/1) and is given for some time period (usually one or four hours).

Other terms occasionally used are:

— **LD_{LO} (Lethal Dose Low)** — The lowest dose of a substance introduced by any route other than inhalation reported to have caused death in humans or animals.

— **LC_{LO} (Lethal Concentration Low)** — The lowest concentration of a substance in air that has been reported to have caused death in humans or animals.

— **TD_{LO} (Toxic Dose Low)** — The lowest dose of a substance to which humans or animals have been exposed and reported to produce a toxic effect other than cancer.

Based on these values, an estimate of human health effects potential is obtained.

Section X — *Transportation Information*

In the event the material is regulated as hazardous by the Department of Transportation (DOT), the Hazardous Materials Regulations as described in the Code of Federal Regulations, 49 Chapter 1 subchapter C are outlined in the LAND portion of Section X. The IMO and IATA/ICAO regulations are also given for water and air modes respectively.

Section XI — *Spill and Leak Procedures*

In the event of an emergency, CHEMTREC (Chemical Transportation Emergency Center) should be contacted.

CHEMTREC is a national center established by the Chemical Manufacturer Association (CMA) in Washington, DC, to relay pertinent emergency information concerning specific chemicals on request. CHEMTREC has a 24-hour toll-free telephone number (800)424-9300, intended primarily for use by those who respond to chemical transportation emergencies.

During cleanup of spills or leaks, it may be necessary to use extra personal protective equipment as compared to normal operations. Recommendations for equipment use additional to what is described in Section V are given.

Procedural recommendations relative to air, land and water are described.

Section XII — *Waste Disposal*

This section gives guidelines for disposing of a product if it becomes a waste. Recommendations are based upon the physical state and hazardous properties of the material. If the material is designated as hazardous by 40 CFR Part 261, it must be disposed of in a permitted hazardous waste treatment, storage, or disposal facility in accordance with local, state, and federal regulations. If the material is non-hazardous, recommendations for disposal are made depending on the physical state and known characteristics of the material.

Section XIII — *Additional Regulatory Information*

This section contains information relevant to compliance with other Federal and/or state laws such as TSCA, FIFRA and FDA.

Section XIV — *Additional Information*

Any relevant additional information is given in this section.

Section XV — *Major References*

This section lists some of the major references that have been consulted in preparing the Material Safety Data Sheet.

Version 3.

Olin CORPORATION

501 Merritt 7, P.O. Box 4500, Norwalk, CT 06856-4500

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MATERIAL SAFETY DATA

OCEAN NETWORK EMERGENCY PHONE 1-800-OLIN-911

THIS MATERIAL SAFETY DATA SHEET (MSDS) HAS BEEN PREPARED IN COMPLIANCE WITH THE FEDERAL OSHA HAZARD COMMUNICATION STANDARD,29 CFR 1910.1200.THIS PRODUCT MAY BE CONSIDERED TO BE A HAZARDOUS CHEMICAL UNDER THAT STANDARD,(REFER TO THE OSHA CLASSIFICATION IN SEC.I.)THIS INFORMATION IS REQUIRED TO BE DISCLOSED FOR SAFETY IN THE WORKPLACE.THE EXPOSURE TO THE COMMUNITY,IF ANY,IS QUITE DIFFERENT.

I. PRODUCT IDENTIFICATION

REVISION NO : 10
REVISION DATE : 1/26/90
PRODUCT CODE : CPE134075
FILE NUMBER : CPE00295.0002
PRODUCT NAME: MONOMETHYLHYDRAZINE
SYNONYMS: MMH, methyl hydrazine
CHEMICAL FAMILY: Hydrazine
FORMULA: CH_6N_2
USE DESCRIPTION: Propellant
OSHA HAZARD CLASSIFICATION: Corrosive; carcinogen; highly toxic, sensitizer; liver, kidney, nervous system, blood, reproductive and lung toxin; skin and eye hazard; flammable

II. COMPONENT DATA

PRODUCT COMPOSITION:
CAS or CHEMICAL NAME: Monomethylhydrazine
CAS NUMBER: 60-34-4
PERCENTAGE RANGE: 95-99%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:	None		None	
CEILING:	0.2	0.35	0.2	0.38
STEL:	None		None	

CAS or CHEMICAL NAME: Water
CAS NUMBER: 7732-18-5
PERCENTAGE RANGE: 1-5%
HAZARDOUS PER 29 CFR 1910.1200: No
EXPOSURE STANDARDS: None Established

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III. PRECAUTIONS FOR SAFE HANDLING AND STORAGE

DO NOT TAKE INTERNALLY. AVOID CONTACT WITH SKIN, EYES AND CLOTHING. UPON CONTACT WITH SKIN OR EYES, WASH OFF WITH WATER.

STORAGE CONDITIONS: Store away from heat, sparks, open flame and oxidants. Store only in well ventilated areas. Do not contaminate. All containers and handling equipment for monomethylhydrazine should be electrically grounded. An inert atmosphere must be maintained over monomethylhydrazine at all times. Nitrogen has been adopted as the padding material for monomethylhydrazine storage and transfer.
DO NOT STORE AT TEMPERATURES ABOVE: 51 Deg.C (124 Deg.F)
OTHER: DO NOT EXPOSE TO DIRECT LIGHT.

PRODUCT STABILITY AND COMPATIBILITY
SHELF LIFE LIMITATIONS: At least one year if stored sealed from air under a nitrogen pad.
INCOMPATIBLE MATERIALS FOR PACKAGING: Package only in 304 or 347 stainless steel containing less than 1% molybdenum
INCOMPATIBLE MATERIALS FOR STORAGE OR TRANSPORT: Oxidizing agents, metal oxides, metals other than low-molybdenum (<1%) stainless steel, and organic materials with high surface area such as rags, cotton waste, sawdust, etc.

IV. PHYSICAL DATA

APPEARANCE: Clear, colorless liquid
FREEZING POINT: -52.4 Deg.C (-62.3 Deg.F)
BOILING POINT: 87.5 Deg.C (189.5 Deg.F)
DECOMPOSITION TEMPERATURE: 88 Deg.C (190 Deg.F)
SPECIFIC GRAVITY: 0.87
BULK DENSITY: 0.874 (g/cc)
pH @ 25 DEG.C: 11-11.5 (5% in neutral distilled water)
VAPOR PRESSURE @ 25 DEG.C: 49.6 mm Hg
SOLUBILITY IN WATER: Completely miscible
VOLATILES, PERCENT BY VOLUME: 100
EVAPORATION RATE: No Data
VAPOR DENSITY: 1.59 (air=1.0)
MOLECULAR WEIGHT: 46.08
ODOR: Amine
COEFFICIENT OF OIL/WATER DISTRIBUTION: No Data

V. PERSONAL PROTECTIVE EQUIPMENT REQUIREMENTS

PERSONAL PROTECTION FOR ROUTINE USE OF PRODUCT:
RESPIRATORY PROTECTION: Wear a NIOSH/MSHA approved respirator if any exposure occurs.

VENTILATION: Use local exhaust ventilation to maintain levels to below the TLV.

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Olin MATERIAL SAFETY DATA

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SKIN PROTECTIVE EQUIPMENT: Wear gloves, boots, apron and a face shield with safety glasses. A full impermeable suit is recommended if exposure is possible to large portion of body.

OTHER: An eye wash and safety shower must be immediately available in area where materials are handled.

EQUIPMENT SPECIFICATIONS (WHEN APPLICABLE):

RESPIRATOR TYPE:	NIOSH/MSHA approved full-face positive-pressure supplied air respirator
GLOVE TYPE:	Viton
BOOT TYPE:	Viton
APRON TYPE:	Viton
PROTECTIVE SUIT:	Viton

VI. FIRE AND EXPLOSION HAZARD INFORMATION

FLAMMABILITY DATA:

FLAMMABLE:	Yes
COMBUSTIBLE:	Not Applicable
PYROPHORIC:	No

FLASH POINT: 21 Deg.C (70 Deg.F) Test Method: Cleveland Open Cup
AUTOIGNITION TEMPERATURE: 194 Deg.C (382 Deg.F)
FLAMMABLE LIMITS AT NORMAL ATMOSPHERIC TEMPERATURE AND PRESSURE (PERCENT VOLUME IN AIR): LEL - 2.5% UEL - 98%

NFPA RATINGS:

HEALTH:	3
FLAMMABILITY:	3
REACTIVITY:	2

HMIS RATINGS:

HEALTH:	3
FLAMMABILITY:	3
REACTIVITY:	2

EXTINGUISHING MEDIA: Carbon dioxide, dry chemical, water spray

FIRE FIGHTING TECHNIQUES AND COMMENTS: Use water to cool containers exposed to fire. See Section XI for protective equipment for fire fighting.

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VII. REACTIVITY INFORMATION

Name: D. FARMER

CONDITIONS UNDER WHICH THIS PRODUCT MAY BE UNSTABLE:

TEMPERATURES ABOVE: 88 Deg.C (190 Deg.F)

MECHANICAL SHOCK OR IMPACT: No

ELECTRICAL (STATIC) DISCHARGE: Yes

HAZARDOUS POLYMERIZATION: Will not occur

INCOMPATIBLE MATERIALS: Avoid contact between monomethylhydrazine and strong oxidizers such as hydrogen peroxide, nitrogen tetroxide, fluorine, halogen fluorides, and fuming nitric acid. Such contact will result in immediate ignition or explosion. Avoid contact with metal oxides such as those of iron, copper, lead, manganese, and molybdenum. Contact with such metal oxide surfaces may lead to flaming decomposition. Avoid contact with organic materials having large surface areas or porous surfaces. Adsorption of monomethylhydrazine by rags, cotton waste, sawdust or similar organic materials will eventually result in spontaneous ignition.

HAZARDOUS DECOMPOSITION PRODUCTS: Carbon monoxide, nitrogen oxides

OTHER CONDITIONS TO AVOID: Exposure to direct sunlight

SUMMARY OF REACTIVITY:

OXIDIZER:	No
PYROPHORIC:	No
ORGANIC PEROXIDE:	No
WATER REACTIVE:	No

VIII. FIRST AID

EYES: Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Call a physician at once.

SKIN: Immediately flush with water for at least 15 minutes. Call a physician. If clothing comes in contact with the product, the clothing should be removed immediately and should be laundered before re-use.

INGESTION: Immediately drink large quantities of water. Induce vomiting. Call a physician at once. DO NOT give anything by mouth if the person is unconscious or if having convulsions.

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Olin MATERIAL SAFETY DATA

INHALATION: If person experiences nausea, headache or dizziness, person should stop work immediately and move to fresh air until these symptoms disappear. If breathing is difficult, administer oxygen, keep the person warm and at rest. Call a physician. In the event that an individual inhales enough vapor to lose consciousness, person should be moved to fresh air at once and a physician should be called immediately. If breathing has stopped, artificial respiration should be given immediately. In all cases, ensure adequate ventilation and provide respiratory protection before the person returns to work.

IX. TOXICOLOGY AND HEALTH INFORMATION

ROUTES OF ABSORPTION

Inhalation, dermal, ingestion, eye contact

WARNING STATEMENTS AND WARNING PROPERTIES

MAY BE FATAL IF INHALED, ABSORBED THROUGH SKIN OR INGESTED. HARMFUL IF EXPOSED TO EYES.

HUMAN THRESHOLD RESPONSE DATA

ODOR THRESHOLD: 1.7 ppm
IRRITATION THRESHOLD: This value has not been established.
IMMEDIATELY DANGEROUS TO LIFE OR HEALTH: 5 ppm

SIGNS, SYMPTOMS, AND EFFECTS OF EXPOSURE

INHALATION

ACUTE:

Monomethyl hydrazine is highly irritating to the nose, throat, upper respiratory tract and lungs. Inflammation of the respiratory tract may lead to bronchitis. Vapor can also cause eye irritation. Pulmonary edema and lung damage may occur. Damage may also result to liver, kidneys and blood. High exposure may give rise to hemolysis of the blood cells. Vomiting, diarrhea, nausea, dizziness, cyanosis and convulsions may also occur. A single exposure would not likely produce fetal toxicity and malformations, but several exposures may cause these effects to the fetus.

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CHRONIC:
The repeated inhalation of monomethyl hydrazine may produce inflammation of the nasal, tracheal and bronchial tissue. Chronic bronchitis can result. Damage to the liver, kidneys, and blood may also occur. Damage to blood may be characterized by hemolysis and reduction of packed cell volume. Fetal toxicity and malformations can also result. Repeated inhalation may produce cancer.

SKIN
ACUTE:
Monomethyl hydrazine by this route can produce severe irritation and/or burns. Dermatitis may also occur. Other effects would be similar to those which may result from inhalation except for those relating specifically to respiratory tract irritation.
CHRONIC:
Repeated exposure can cause an allergic reaction resulting in dermatitis and a characteristic rash. Other effects would be similar to those described under chronic inhalation exposure except for those relating specifically to respiratory tract irritation.

EYE
Exposure can cause inflammation, swelling, redness, and discharge. Temporary blindness can occur. If not rinsed immediately from the eyes, burns and permanent corneal damage can occur resulting in impairment of vision.

INGESTION
ACUTE:
Irritation and/or burns can occur to the entire gastrointestinal tract, including the stomach and intestines, characterized by nausea, vomiting, diarrhea, abdominal pain, bleeding, and/or tissue ulcerstion. The other effects would be similar as stated under inhalation exposure, including those to the respiratory tract, if vapor is inhaled.
CHRONIC:
Inflammation to the gastrointestinal tract can occur. Other effects would be similar as stated under inhalation exposure including those to the respiratory tract if vapor is inhaled.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE
Diseases of the liver, kidneys, and blood, as well as asthma and cardiovascular disease.

INTERACTIONS WITH OTHER CHEMICALS WHICH ENHANCE TOXICITY
None known or reported

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Olin MATERIAL SAFETY DATA

ANIMAL TOXICOLOGY

ACUTE TOXICITY:
Inhalation LC 50: 74 ppm (4 hr. exposure, rat); 427 ppm (rats, 30 minutes)
Dermal LD 50: 93 mg/kg (rabbit)
Oral LD 50: 71 mg/kg (rat)
Irritation: Corrosive to skin and eyes

ACUTE TARGET ORGAN TOXICITY:
Damage to lungs, liver, kidneys, blood and central nervous system.

CHRONIC TARGET ORGAN TOXICITY:
Repeated exposure to monomethyl hydrazine has produced damage to the lungs, liver, kidneys, and blood. Cancer has also been observed in laboratory animals.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY:
Monomethyl hydrazine has been shown to produce embryo lethality and fetal malformations in laboratory animals.

CARCINOGENICITY:
Monomethyl hydrazine is recognized as a cancer-causing agent in animals by IARC and OSHA. It is considered a suspect carcinogen in humans by these two organizations.

MUTAGENICITY:
Monomethyl hydrazine has been shown to cause DNA and chromosomal damage in a number of test systems. It is considered mutagenic.

AQUATIC TOXICITY:
There is no available data on toxicity to aquatic organisms.

X. TRANSPORTATION INFORMATION

THIS MATERIAL IS REGULATED AS A DOT HAZARDOUS MATERIAL.

DOT DESCRIPTION FROM THE HAZARDOUS MATERIALS TABLE 49 CFR 172.101:
METHYLHYDRAZINE FLAMMABLE LIQUID UN 1244 POISON - INHALATION HAZARD

REPORTABLE QUANTITY: 10 lbs. (Per 49 CFR 172.101, Appendix)

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The material described above is subject to the U.S. DOT HAZARDOUS MATERIALS REGULATIONS via the modes and packaging quantities indicated below.

MODE:		PACKAGING QUANTITIES:			
__x__	Rail	__x__	Bulk	__x__	Non-Bulk
__x__	Motor	__x__	Bulk	__x__	Non-Bulk
__x__	Water	__x__	Bulk	__x__	Non-Bulk
__x__	Air	__x__	Bulk	__x__	Non-Bulk

The applicable packaging section in 49 CFR is 173.145.

XI. SPILL AND LEAKAGE PROCEDURES

FOR ALL TRANSPORTATION ACCIDENTS, CALL CHEMTREC AT 800-424-9300.

REPORTABLE QUANTITY: Per 40 CFR 302.4 as monomethylhydrazine (10 lbs.)

SPILL MITIGATION PROCEDURES:
Evacuation procedures must be placed into effect. Hazardous concentrations in air may be found in local spill area and immediately downwind. Utilize emergency response personal protective equipment prior to the start of any response. Remove all sources of ignition. Stop source of spill as soon as possible and notify appropriate personnel.

AIR RELEASE: Vapors may be suppressed by the use of water fog. Contain all liquid for treatment or neutralization.

WATER RELEASE: This material is lighter than and miscible in water. Notify all downstream water users of possible contamination. Divert water flow around spill if possible and safe to do so. Remove with a vacuum system or pumping device for treatment and/or disposal. Continue to handle as described in land spill.

LAND SPILL: Create a dike or trench to contain materials. Begin to neutralize material using a 5% hypochlorite solution but add only after original spill materials have been reduced to a 5% or less concentrated solution. Do not place spill materials back in their original container. Containerize and label all spill materials properly. Decontaminate all clothing and the spill area using a detergent and flush with large amounts of water.
Addition of water to dilute material below 30% will greatly reduce potential fire hazards.

SPILL RESIDUES:
Dispose of per guidelines under Section XII, WASTE DISPOSAL.

This material may be neutralized for disposal; you are requested to contact OCEAN at 800-OLIN-911 before beginning any such operation.

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Olin MATERIAL SAFETY DATA

PERSONAL PROTECTION FOR EMERGENCY SPILL AND FIRE-FIGHTING SITUATIONS:
In case of fire, use normal fire fighting equipment.

Additional respiratory protection is necessary when a spill or fire involving this product occurs. You are recommended to use a self-contained breathing apparatus (SCBA) positive pressure unit.

Response to this material may require the use of a full encapsulated suit and self-contained breathing apparatus (SCBA).

Additional protective clothing must be worn to prevent personal contact with this material. Those items include but are not limited to boots, gloves, hard hat, splash-proof goggles and impervious clothing, i.e., chemically impermeable suit.

Compatible materials for response to this material are neoprene and butyl rubber.

Protection concerns must also address the potential of the physical characteristics of this product as poison by Inhalation

XII. WASTE DISPOSAL

If this product becomes a waste, it meets the criteria of a hazardous waste as defined under 40 CFR 261 and would have the following EPA hazardous waste number: D001, P068.

If this product becomes a waste, it will be a hazardous waste which is subject to the Land Disposal Restrictions under 40 CFR 268 and must be managed accordingly.

As a hazardous liquid waste, it must be disposed of in accordance with local, state and federal regulations in a permitted hazardous waste treatment, storage and disposal facility by incineration.

CARE MUST BE TAKEN TO PREVENT ENVIRONMENTAL CONTAMINATION FROM THE USE OF THIS MATERIAL. THE USER OF THIS MATERIAL HAS THE RESPONSIBILITY TO DISPOSE OF UNUSED MATERIAL, RESIDUES AND CONTAINERS IN COMPLIANCE WITH ALL RELEVANT LOCAL, STATE AND FEDERAL LAWS AND REGULATIONS REGARDING TREATMENT, STORAGE AND DISPOSAL FOR HAZARDOUS AND NONHAZARDOUS WASTES.

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XIII. ADDITIONAL REGULATORY STATUS INFORMATION

TOXIC SUBSTANCES CONTROL ACT:
This substance is listed on the Toxic Substances Control Act inventory.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 - PROPOSITION 65:
"WARNING: This product contains detectable amounts of a chemical known to the State of California to cause cancer and birth defects or other reproductive harm."

SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT TITLE III:
HAZARD CATEGORIES, PER 40 CFR 370.2:
HEALTH:
Immediate (Acute)
Delayed (Chronic)
PHYSICAL:
Fire

EMERGENCY PLANNING AND COMMUNITY RIGHT TO KNOW, PER 40 CFR 355, APP. A:
EXTREMELY HAZARDOUS SUBSTANCES - THRESHOLD PLANNING QUANTITY:
500 lbs.
SUPPLIER NOTIFICATION REQUIREMENTS, PER 40 CFR 372.45:
This mixture or tradename product contains a toxic chemical or chemicals subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40CFR372.

Chemicals listed are: Monomethylhydrazine

XIV. ADDITIONAL INFORMATION

No Additional Information

XV. MAJOR REFERENCES

1. ACGIH Guide to Protective Clothing. Cincinnati, OH: American Conference of Government Industrial Hygienists, 1987.
2. ANSI Z88.2. Recommended Practice for Respiratory Protection. American National Standards Institute, New York, NY.
3. Baker, C. J., The Fire Fighter's Handbook of Hazardous Materials, 4th Ed., Indiana: Maltese Enterprises, Inc., 1984.
4. Bretherick, L., Handbook of Reactive Chemical Hazards, 3rd Ed., Boston, MA: Butterworths, 1985.
5. Casarett, L. and J. Doull, Eds., Toxicology: The Basic Science of Poisons, 3rd Ed., New York: Macmillan Publishing Co., Inc. 1986.
6. CERIS (Chemical Emergency Response Information System) On Line Database. Association of American Railroads.
7. Chemical Degradation and Permeation Database and Selection Guide for Resistant Protective Materials. Austin, TX.

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Olin MATERIAL SAFETY DATA

8. Clayton, G. and F. Clayton, Eds., Patty's Industrial Hygiene and Toxicology, Vol. 2A-C 3rd Ed., New York: John Wiley & Sons, 1981-1982.
9. Code of Federal Regulations, Titles 21, 29, 40 and 49. Washington, DC: U.S. Government Printing Office.
10. Fire Protection Guide on Hazardous Materials, 9th Ed., National Fire Protection Association, Batterymarch Park, Quincy, MA, 1986.
11. Gosselin, R., et al., Gosselin-Clinical Toxicology of Commercial Products, 5th Ed., Baltimore: Williams and Wilkins, 1984.
12. Grant, W. Morton, M.D., Toxicology of the Eye, 2nd Ed., Springfield, IL: Charles C. Thomas, 1974.
13. Hazardline, Occupational Health Services Inc., New York, NY.
14. IARC Monogram on the Evaluation of Carcinogenic Risk of Chemicals to Man., Geneva: World Health Organization; International Agency for Research on Cancer.
15. Lenga, R., The Sigma-Aldrich Library of Chemical Safety Data, 1st Ed., Milwaukee, WI: Sigma-Aldrich Corporation, 1985.
16. Lewis, R. and D. Sweet, Eds., Registry of Toxic Effects of Chemical Substances, 1985-1986, Washington, DC: U.S. Government Printing Office, 1987.
17. Medline, U.S. National Library of Medicine, Bethesda, MD.
18. McKee, Jack E. and Harold W. Wolf, Eds., Water Quality Criteria, NTIS PB Report; (PB-82-188244), 2nd Ed., Springfield, VA: National Technical Information Services, 1963.
19. NIOSH Pocket Guide to Chemical Hazards. Washington, DC: U.S. Government Printing Office, 1985.
20. Olin Respiratory Protection Manual.
21. Sax, N. Irving, Dangerous Properties of Hazardous Materials 6th Ed., New York: Van Nostrand Reinhold Company, 1984.
22. Threshold Limit Values and Biological Exposure Indices for 1989-90. Cincinnati, OH: American Conference of Government Industrial Hygienists, 1989.
23. Toxic Substances Control Act Inventory, Washington, DC: U.S. Government Printing Office, 1986.
24. Back, K. C. et al. April, 1978. Occupational Hazards of Missile Operations with Special Regard to the Hydrazine Propellants. Aviat. Space Environ. Med., 49(4):591-598.
25. Coe, F. L. et al. July, 1967. The Effects of Monomethylhydrazine upon Renal Function. USAF School of Aerospace Medicine. Aerospace Medical Division (AFSC). Brooks Air Force Base, TX. SAM-TR-67-61.
26. Jacobson, K. H. et al. April, 1955. The Acute Toxicity of the Vapors of Some Methylated Hydrazine Derivatives. A. M. A. Archives of Industrial Health. pp. 609-616.

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27. Keller, W. C. et al. 1984. Teratogenic Assessment of Three Methylated Hydrazine Derivatives in the Rat. Journal of Toxicology and Environmental Health, 13:125-131.
28. Simon, C. W. December 29, 1967. Monomethyl Hydrazine - A Summary of the Literature. C7-3197/501.
29. Simon, C. W. and Squillace, A. S. December 29, 1967. Monomethyl Hydrazine Vapor Exposure Limits for the Minuteman III Missile System. C7-3198/501. AF04(694)-786.
30. Sopher, R. L. et al. January, 1969. Renal Pathology of Acute Methylhydrazine Intoxication in Dogs. Aerospace Medicine, 40(1):55-61.
31. Toth, B. 1988. Toxicities of Hydrazines: A Review. In Vivo. 2:209-242.
32. Van Stee, E. W. 1965. Acute Effects of Exposure to Hydrazine and Hydrazine Derivatives on Renal Function in the Dog. Aerospace Medicine. pp. 764-767.

THE INFORMATION IN THIS MATERIAL SAFETY DATA SHEET SHOULD BE PROVIDED TO ALL WHO WILL USE, HANDLE, STORE, TRANSPORT, OR OTHERWISE BE EXPOSED TO THIS PRODUCT. THIS INFORMATION HAS BEEN PREPARED FOR THE GUIDANCE OF PLANT ENGINEERING, OPERATIONS AND MANAGEMENT AND FOR PERSONS WORKING WITH OR HANDLING THIS PRODUCT. OLIN BELIEVES THIS INFORMATION TO BE RELIABLE AND UP TO DATE AS OF THE DATE OF PUBLICATION, BUT MAKES NO WARRANTY THAT IT IS. ADDITIONALLY, IF THIS MATERIAL SAFETY DATA SHEET IS MORE THAN THREE YEARS OLD, YOU SHOULD CONTACT OLIN AT THE PHONE NUMBER LISTED BELOW TO MAKE CERTAIN THAT THIS SHEET IS CURRENT.

OLIN MSDS CONTROL GROUP
Olin Corporation
120 Long Ridge Road
Stamford, CT 06904

Phone Number: (203) 356-3449

OLIN CORPORATION SUBSIDIARIES AND AFFILIATED ENTITIES: ASAHI-OLIN LTD., BRIDGEPORT BRASS CORPORATION, INDY ELECTRONICS, INC., OLIN CHLORATE CORPORATION, OLIN FABRICATED METAL PRODUCTS INC., OLIN HUNT SPECIALTY PRODUCTS INC., OLIN ELECTRONICS TECHNOLOGY, OLIN MESA CORP., OLIN SPECIALTY METALS CORPORATION, PACIFIC ELECTRO DYNAMICS, INC., PHYSICS INTERNATIONAL COMPANY, ROCKET RESEARCH COMPANY.

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.ORIG

TO: ROCKWELL INTERNATIONAL
ATTN: KIM TAVASOLI
X XX

OLIN CORPORATION
Material Safety Data Sheet

04/09/96

FOR FURTHER INFORMATION (OTHER THAN EMERGENCIES) CALL:

(800) 511-MSDS

Product Name: MONOMETHYLHYDRAZINE
Product Code: CPE810002
MSDS Number : CPE00295.0003

OCEAN NETWORK EMERGENCY PHONE 1-800-OLIN-911

This Material Safety Data Sheet (MSDS) has been prepared in compliance with the Federal OSHA Hazard Communication Standard,29 CFR 1910.1200. This product may be considered to be a hazardous chemical under that standard. (Refer to the OSHA classification in SEC.I.)This information is required to be disclosed for safety in the workplace. The exposure to the community, if any, is quite different.

I. PRODUCT IDENTIFICATION

REVISION NUMBER : 08
REVISION DATE : 02/06/96
MSDS FILE NUMBER: CPE00295.0003
PRODUCT CODE : 810002
MSDS NAME : MONOMETHYLHYDRAZINE

SYNONYMS: MMH, methyl hydrazine
CHEMICAL FAMILY: Hydrazine
FORMULA: CH\6N\2
USE DESCRIPTION: Propellant
OSHA HAZARD CLASSIFICATION: Corrosive; suspect carcinogen; highly toxic; sensitizer; liver, kidney, nervous system, blood and lung toxin; skin and eye hazard; flammable liquid

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II. COMPONENT-DATA

PRODUCT COMPOSITION:
CAS or CHEMICAL NAME: Monomethylhydrazine
CAS NUMBER: 60-34-4
PERCENTAGE RANGE: 95-99%
HAZARDOUS PER 29 CFR 1910.1200: Yes
EXPOSURE STANDARDS:

	OSHA(PEL)		ACGIH(TLV)	
	ppm	mg/cubic-meter	ppm	mg/cubic-meter
TWA:	None		0.01	0.019 (skin)
CEILING:	0.2	0.35 (skin)	None	
STEL:	None		None	

CAL OSHA .2

CAS or CHEMICAL NAME: Water
CAS NUMBER: 7732-18-5
PERCENTAGE RANGE: 1-5%
HAZARDOUS PER 29 CFR 1910.1200: No
EXPOSURE STANDARDS: None Established

III. SAFE HANDLING AND STORAGE

DO NOT TAKE INTERNALLY. AVOID CONTACT WITH SKIN, EYES AND CLOTHING. UPON CONTACT WITH SKIN OR EYES, WASH OFF WITH WATER. DO NOT BREATHE VAPOR OR MIST.
STORAGE CONDITIONS: Store away from heat, sparks, open flame and oxidants. Store only in well ventilated areas. Do not contaminate. All containers and handling equipment for monomethylhydrazine should be electrically grounded. An inert atmosphere must be maintained over monomethylhydrazine at all times. Nitrogen has been adopted as the padding material for monomethylhydrazine storage and transfer.
DO NOT STORE AT TEMPERATURES ABOVE: 51 Deg.C (124 Deg.F)
OTHER: DO NOT EXPOSE TO DIRECT LIGHT.

PRODUCT STABILITY AND COMPATIBILITY
SHELF LIFE LIMITATIONS: 5 Years if not opened and exposed to the atmosphere. Material older than 5 years should be retested before use.
INCOMPATIBLE MATERIALS FOR PACKAGING: Package only in 304 or 347 stainless steel containing less than 1% molybdenum
INCOMPATIBLE MATERIALS FOR STORAGE OR TRANSPORT: Oxidizing agents, metal oxides, metals other than low-molybdenum (<1%) stainless steel, and organic materials with high surface area such as rags, cotton waste, sawdust, etc.

IV. PHYSICAL DATA

APPEARANCE: Clear, colorless liquid
FREEZING POINT: -52.4 Deg.C (-62.3 Deg.F)
BOILING POINT: 87.5 Deg.C (189.5 Deg.F)
DECOMPOSITION TEMPERATURE: 88 Deg.C (190 Deg.F)
SPECIFIC GRAVITY: 0.87
BULK DENSITY: 0.874 (g/cc)
pH @ 25 DEG.C: 11-11.5 (5% in neutral distilled water)
VAPOR PRESSURE @ 25 DEG.C: 49.6 mm Hg
SOLUBILITY IN WATER: Completely miscible
VOLATILES, PERCENT BY VOLUME: 100
EVAPORATION RATE: No Data
VAPOR DENSITY: 1.59 (air=1.0)

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MOLECULAR WEIGHT: 46.08
ODOR: Amine
COEFFICIENT OF OIL/WATER DISTRIBUTION: No Data
MONOMETHYLHYDRAZINE CPE810002 PAGE 3

V. PERSONAL PROTECTIVE EQUIP

PERSONAL PROTECTION FOR ROUTINE USE OF PRODUCT:
RESPIRATORY PROTECTION: Wear a NIOSH/MSHA approved respirator if any exposure occurs.
VENTILATION: Use explosion-proof local exhaust ventilation to maintain levels to below the TLV.

SKIN PROTECTIVE EQUIPMENT: Wear gloves, boots, apron and a face shield with safety goggles. A full impermeable suit is recommended if exposure is possible to large portion of body.

OTHER: An eye wash and safety shower must be immediately available in area where materials are handled.

EQUIPMENT SPECIFICATIONS (WHEN APPLICABLE):

RESPIRATOR TYPE:	NIOSH/MSHA approved full-face positive-pressure supplied air respirator
GLOVE TYPE:	Butyl rubber
BOOT TYPE:	Butyl rubber
APRON TYPE:	Butyl rubber
PROTECTIVE SUIT:	Butyl rubber

VI. FIRE & EXPLOSION HAZARDS

FLAMMABILITY DATA:

FLAMMABLE:	Yes
COMBUSTIBLE:	Not Applicable
PYROPHORIC:	No

FLASH POINT: 21 Deg.C (70 Deg.F) Test Method: Cleveland Open Cup
AUTOIGNITION TEMPERATURE: 194 Deg.C (382 Deg.F)
FLAMMABLE LIMITS AT NORMAL ATMOSPHERIC TEMPERATURE AND PRESSURE (PERCENT VOLUME IN AIR): LEL - 2.5% UEL - 98%

NFPA RATINGS:

HEALTH:	4
FLAMMABILITY:	3
REACTIVITY:	2

HMIS RATINGS:

HEALTH:	3
FLAMMABILITY:	3
REACTIVITY:	2

EXTINGUISHING MEDIA: Carbon dioxide, dry chemical, water spray

FIRE FIGHTING TECHNIQUES AND COMMENTS: Use water to cool containers exposed to fire. See Section XI for protective equipment for fire fighting.

VII. REACTIVITY

CONDITIONS UNDER WHICH THIS PRODUCT MAY BE UNSTABLE:
TEMPERATURES ABOVE: 88 Deg.C (190 Deg.F)

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MECHANICAL SHOCK OR IMPACT: No
ELECTRICAL (STATIC) DISCHARGE: Yes
HAZARDOUS POLYMERIZATION: Will not occur

INCOMPATIBLE MATERIALS: Avoid contact between monomethylhydrazine and strong oxidizers such as hydrogen peroxide, nitrogen tetroxide, fluorine, halogen fluorides, and fuming nitric acid. Such contact will result in immediate ignition or explosion. Avoid contact with metal oxides such as those of iron, copper, lead, manganese, and molybdenum. Contact with such metal oxide surfaces may lead to flaming decomposition. Avoid contact with organic materials having large surface areas or porous surfaces. Adsorption of monomethylhydrazine by rags, cotton waste, sawdust or similar organic materials will eventually result in spontaneous ignition.
HAZARDOUS DECOMPOSITION PRODUCTS: Carbon monoxide, nitrogen oxides
OTHER CONDITIONS TO AVOID: Exposure to direct sunlight

SUMMARY OF REACTIVITY:

OXIDIZER:	No
PYROPHORIC:	No
ORGANIC PEROXIDE:	No
WATER REACTIVE:	No

VIII. FIRST AID

EYES: Immediately flush with large amounts of water for at least 15 minutes, occasionally lifting the upper and lower eyelids. Call a physician at once.

SKIN: Immediately flush with water for at least 15 minutes. Call a physician. If clothing comes in contact with the product, the clothing should be removed immediately and should be laundered before re-use.

INGESTION: Immediately drink large quantities of water. Induce vomiting. Call a physician at once. DO NOT give anything by mouth if the person is unconscious or if having convulsions.

INHALATION: If person experiences nausea, headache or dizziness, person should stop work immediately and move to fresh air until these symptoms disappear. If breathing is difficult, administer oxygen, keep the person warm and at rest. Call a physician. In the event that an individual inhales enough vapor to lose consciousness, person should be moved to fresh air at once and a physician should be called immediately. If breathing has stopped, artificial respiration should be given immediately. In all cases, ensure adequate ventilation and provide respiratory protection before the person returns to work.

IX. TOXICOLOGY & HEALTH

ROUTES OF ABSORPTION
Inhalation, dermal, ingestion, eye contact

WARNING STATEMENTS AND WARNING PROPERTIES
MAY BE FATAL IF INHALED, ABSORBED THROUGH SKIN OR INGESTED. CAUSES EYE, SKIN, DIGESTIVE TRACT AND RESPIRATORY TRACT BURNS. CAUSES LIVER, KIDNEY, BLOOD, LUNG AND NERVOUS SYSTEM DAMAGE. MAY CAUSE AN ALLERGIC SKIN

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REACTION. MAY CAUSE CANCER BASED ON ANIMAL DATA.

ODOR THRESHOLD: 1.7 ppm
IRRITATION THRESHOLD: This value has not been established.
IMMEDIATELY DANGEROUS TO LIFE OR HEALTH: 20 ppm

SIGNS, SYMPTOMS, AND EFFECTS OF EXPOSURE

INHALATION
ACUTE:
Monomethylhydrazine is highly toxic and rapidly absorbed through the lungs. It is highly irritating to the nose, throat, upper respiratory tract and lungs. Inflammation of the respiratory tract may lead to bronchitis. Pulmonary edema and lung damage may occur. Damage may also result to liver, kidneys and blood. High exposure may give rise to hemolysis of the blood cells. Vomiting, diarrhea, nausea, dizziness, cyanosis and convulsions may also occur. Significant exposures to this product could result in serious health effects and/or death.

CHRONIC:
The repeated inhalation of monomethyl hydrazine may produce inflammation of the nasal, tracheal and bronchial tissue. Chronic bronchitis can result. Damage to the liver, kidneys, and blood may also occur. Damage to blood may be characterized by hemolysis and reduction of packed cell volume. Repeated inhalation of monomethylhydrazine has produced cancer in laboratory animals.

SKIN
ACUTE:
Monomethylhydrazine is rapidly absorbed through the skin and is highly toxic by this route which is dependent on exposed skin surface area and concentration of the solution. Exposure to large areas of the skin may lead to a significant dose being absorbed causing systemic toxicity similar to the effects described for inhalation exposure and possibly death. Monomethylhydrazine can produce severe irritation and/or burns.

Dermatitis may also occurs.

CHRONIC:
Repeated exposure can cause an allergic reaction resulting in dermatitis and a characteristic rash. Other effects would be similar to those described under chronic inhalation exposure.

EYE
Exposure can cause inflammation, swelling, redness, and discharge. Temporary blindness can occur. If not rinsed immediately from the eyes, burns and permanent corneal damage can occur resulting in impairment of vision.

INGESTION
ACUTE:
Monomethylhydrazine is highly toxic if ingested. Irritation and/or burns can occur to the entire gastrointestinal tract, including the stomach and intestines, characterized by nausea, vomiting, diarrhea, abdominal pain, bleeding, and/or tissue ulceration. The other effects would be similar as stated under inhalation exposure. Significant exposure to this material could lead to serious health effects and/or death.

CHRONIC:

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Inflammation to the gastrointestinal tract can occur. Other effects would be similar as stated under inhalation exposure. Chronic ingestion has produced cancer in laboratory animals.

MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE
Diseases of the liver, kidneys, and blood, as well as asthma and cardiovascular disease and nervous system disorders.

INTERACTIONS WITH OTHER CHEMICALS WHICH ENHANCE TOXICITY
None known or reported

ANIMAL TOXICOLOGY
ACUTE TOXICITY:
Inhalation LC 50: 74 ppm (4 hr. exposure, rat); 148 ppm (rats, 1 hr)
Dermal LD 50: 93 mg/kg (rabbit)
Oral LD 50: 32 mg/kg (rat)
Irritation: Corrosive to skin and eyes; irritating to the respiratory tract

ACUTE TARGET ORGAN TOXICITY:
Damage to lungs, liver, kidneys, blood and central nervous system.

CHRONIC TARGET ORGAN TOXICITY:
Repeated exposure to monomethyl hydrazine has produced damage to the lungs, liver, kidneys, blood and nervous system. Cancer has also been observed in laboratory animals.

REPRODUCTIVE AND DEVELOPMENTAL TOXICITY:
High concentrations of monomethylhydrazine have produced embryolethality and fetal malformations to the offspring of animals exposed during pregnancy. These findings were only osberved at concentrations that caused significant maternal toxicity. Under industrial use conditions where exposures are kept at or below the recommended occupational exposure standards, exposure to this product should not pose a reproductive or developmental toxicity hazard.

CARCINOGENICITY:
Monomethylhydrazine is not known or reported to be carcinogenic by the following reference sources: IARC, NTP or EPA. Monomethylhydrazine is listed by ACGIH as a suspect human carcinogen, and NIOSH considers it to be a carcinogen defined with no further categorization to human or animal carcinogenicity. Hydrazine and the hydrazine derivative, 1,1-Dimethylhydrazine, have been shown to be carcinogenic in laboratory animals. They are considered to be suspect human carcinogens by IARC, NTP and ACGIH. Based on structural similarity to these compounds and carcinogenic findings in some animal studies, monomethylhydrazine should be handled with care and treated as a suspect carcinogen.

MUTAGENICITY:
Monomethylhydrazine has been shown to cause DNA and chromosomal damage in a number of test systems. It is considered mutagenic.

AQUATIC TOXICITY:
48 hr LC50 (measured, static): 1.2 mg/l (Scud)
96 hr LC50 (measured, static): 3.54 mg/l (Channel Catfish)
96 hr LC50 (measured, static): 2.27 mg/l (Golden shiner)

X. TRANSPORTATION

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THIS MATERIAL IS REGULATED AS A DOT HAZARDOUS MATERIAL.
DOT DESCRIPTION FROM THE HAZARDOUS MATERIALS TABLE 49 CFR 172.101:
MONOMETHYLHYDRAZINE CPE810002 PAGE 7

LAND (U.S.DOT): METHYLHYDRAZINE, 6.1, UN 1244, PG I,
Poison Inhalation Hazard - Hazard Zone A

WATER (IMO): SAME AS LAND (FLASH POINT 21 Deg.C)

AIR (IATA/ICAO): FORBIDDEN

HAZARD LABEL/PLACARD: TOXIC, FLAMMABLE LIQUID, CORROSIVE
REPORTABLE QUANTITY: 10 lbs. (Per 49 CFR 172.101, Appendix)
EMERGENCY GUIDE NUMBER: 57
SPECIAL COMMENTS: Exemptions for 4BW and 110A500W type containers exist for this material. Air shipments may be possible using specialized containers.

XI. SPILL & LEAKAGE

FOR ALL TRANSPORTATION ACCIDENTS, CALL CHEMTREC AT 800-424-9300.

REPORTABLE QUANTITY: This product is subject to a Reportable Quantity with respect to monomethylhydrazine. RQs are subject to change and reference should be made to 40 CFR 302.4 for the current requirements

SPILL MITIGATION PROCEDURES:
Evacuation procedures must be placed into effect. Hazardous concentrations in air may be found in local spill area and immediately downwind. Utilize emergency response personal protective equipment prior to the start of any response. Remove all sources of ignition. Stop source of spill as soon as possible and notify appropriate personnel.
AIR RELEASE: Vapors may be suppressed by the use of water fog. Contain all liquid for treatment or neutralization.
WATER RELEASE: This material is lighter than and miscible in water. Notify all downstream water users of possible contamination. Divert water flow around spill if possible and safe to do so. Remove with a vacuum system or pumping device for treatment and/or disposal. Continue to handle as described in land spill.
LAND SPILL: Create a dike or trench to contain materials. Begin to neutralize material using a 5% hypochlorite solution but add only after original spill materials have been reduced to a 5% or less concentrated solution. Do not place spill materials back in their original container. Containerize and label all spill materials properly. Decontaminate all clothing and the spill area using a detergent and flush with large amounts of water.
Addition of water to dilute material below 30% will greatly reduce potential fire hazards.

SPILL RESIDUES:
Dispose of per guidelines under Section XII. WASTE DISPOSAL.

This material may be neutralized for disposal; you are requested to contact OCEAN at 800-OLIN-911 before beginning any such operation.

PERSONAL PROTECTION FOR EMERGENCY SPILL AND FIRE-FIGHTING SITUATIONS:
Additional respiratory protection is necessary when a spill or fire

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involving this product occurs. You are recommended to use a self-contained breathing apparatus (SCBA) positive pressure unit.

Response to this material may require the use of a full encapsulated suit and self-contained breathing apparatus (SCBA).

Additional protective clothing must be worn to prevent personal contact with this material. Those items include but are not limited to boots, gloves, hard hat, splash-proof goggles, full face shield and impervious clothing, i.e., chemically impermeable suit or a full encapsulated suit.

Compatible material for response to this material is butyl rubber.

Protection concerns must also address the potential of the physical characteristics of this product as poison by inhalation, flammable liquid and corrosive liquid.

XII. WASTE DISPOSAL

If this product becomes a waste, it meets the criteria of a hazardous waste as defined under 40 CFR 261 and would have the following EPA hazardous waste number: D001, P068.

If this product becomes a waste, it will be a hazardous waste which is subject to the Land Disposal Restrictions under 40 CFR 268 and must be managed accordingly.

As a hazardous liquid waste, it must be disposed of in accordance with local, state and federal regulations in a permitted hazardous waste treatment, storage and disposal facility by incineration.
CARE MUST BE TAKEN TO PREVENT ENVIRONMENTAL CONTAMINATION FROM THE USE OF THIS MATERIAL. THE USER OF THIS MATERIAL HAS THE RESPONSIBILITY TO DISPOSE OF UNUSED MATERIAL, RESIDUES AND CONTAINERS IN COMPLIANCE WITH ALL RELEVANT LOCAL, STATE AND FEDERAL LAWS AND REGULATIONS REGARDING TREATMENT, STORAGE AND DISPOSAL FOR HAZARDOUS AND NONHAZARDOUS WASTES.

XIII. ADDITIONAL REG STATUS

TOXIC SUBSTANCES CONTROL ACT:
This substance is listed on the Toxic Substances Control Act inventory.

CALIFORNIA SAFE DRINKING WATER AND TOXIC ENFORCEMENT ACT OF 1986 - PROPOSITION 65:
"WARNING: This product contains detectable amounts of a chemical known to the State of California to cause cancer and birth defects or other reproductive harm."

SUPERFUND AMENDMENTS AND REAUTHORIZATION ACT TITLE III:
HAZARD CATEGORIES, PER 40 CFR 370.2:
HEALTH:
Immediate (Acute)
Delayed (Chronic)
PHYSICAL:
Fire

EMERGENCY PLANNING AND COMMUNITY RIGHT TO KNOW, PER 40 CFR 355, APP. A:
EXTREMELY HAZARDOUS SUBSTANCES - THRESHOLD PLANNING QUANTITY:
500 lbs.

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SUPPLIER NOTIFICATION REQUIREMENTS, PER 40 CFR 372.45:
This mixture or tradename product contains a toxic chemical or chemicals subject to the reporting requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 and 40CFR372.
Chemicals listed are: Monomethylhydrazine

XIV. ADDITIONAL INFORMATION

MSDS REVISION STATUS: Exposure standards, toxicology information and references updated. (10)

XV. MAJOR REFERENCES

1. Back, K. C. et al. April, 1978. Occupational Hazards of Missile Operations with Special Regard to the Hydrazine Propellants. Aviat. Space Environ. Med., 49(4):591-598.
2. Coe, F. L. et al. July, 1967. The Effects of Monomethylhydrazine upon Renal Function. USAF School of Aerospace Medicine. Aerospace Medical Division (AFSC). Brooks Air Force Base, TX. SAM-TR-67-61.
3. Jacobson, K. H. et al. April, 1955. The Acute Toxicity of the Vapors of Some Methylated Hydrazine Derivatives. A. M. A. Archives of Industrial Health. pp. 609-616.
4. Keller, W. C. et al. 1984. Teratogenic Assessment of Three Methylated Hydrazine Derivatives in the Rat. Journal of Toxicology and Environmental Health, 13:125-131.
5. Simon, C. W. December 29, 1967. Monomethyl Hydrazine - A Summary of the Literature. C7-3197/501.
6. Simon, C. W. and Squillace, A. S. December 29, 1967. Monomethyl Hydrazine Vapor Exposure Limits for the Minuteman III Missile System. C7-3198/501. AF04(694)-786.
7. Sopher, R. L. et al. January, 1969. Renal Pathology of Acute Methylhydrazine Intoxication in Dogs. Aerospace Medicine, 40(1):55-61.
8. Toth, B. 1988. Toxicities of Hydrazines: A Review. In Vivo. 2:209-242.
9. Van Stee, E. W. 1965. Acute Effects of Exposure to Hydrazine and Hydrazine Derivatives on Renal Function in the Dog. Aerospace Medicine. pp. 764-767.
10. Toth, B., and H. Shimizu, Methylhydrazine Tumorigenesis in Syrian Golden Hamsters and the Morphology of Malignant Histiocytomas. Cancer Research, Vol. 33, p. 2744 - 2753, November 1973.
11. Haun, C.C., et al., The Acute Inhalation Toxicity of Monomethyl hydrazine Vapor. Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, OH., Document #AMRL-TR-68-169, April 1969.
12. ACGIH Documentation of the Threshold Limit Values and Biological Exposure Indices, 6th Edition, 1991. American Conference of Governmental Industrial Hygienists, Inc., Cincinnati, OH.
13. AQUIRE Database (aquatic toxicity), Chemical Information Systems, Inc. (a division of PSI International, Inc.), Fairfax, VA.
14. TOXNET Database, U.S. National Library of Medicine, Bethesda, MD.

THE INFORMATION IN THIS MATERIAL SAFETY DATA SHEET SHOULD BE PROVIDED TO ALL WHO WILL USE, HANDLE, STORE, TRANSPORT, OR OTHERWISE BE EXPOSED TO THIS PRODUCT. THIS INFORMATION HAS BEEN PREPARED FOR THE GUIDANCE OF PLANT ENGINEERING, OPERATIONS AND MANAGEMENT AND FOR PERSONS WORKING WITH OR HANDLING THIS PRODUCT. OLIN BELIEVES THIS INFORMATION TO BE RELIABLE

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AND UP TO DATE AS OF THE DATE OF PUBLICATION, BUT MAKES NO WARRANTY THAT IT IS. ADDITIONALLY, IF THIS MATERIAL SAFETY DATA SHEET IS MORE THAN THREE YEARS OLD, YOU SHOULD CONTACT OLIN AT THE PHONE NUMBER LISTED BELOW

TO MAKE CERTAIN THAT THIS SHEET IS CURRENT.

OLIN MSDS CONTROL GROUP
Olin Corporation
501 Merritt 7
P.O. Box 4500
Norwalk, CT 06856-4500
Phone Number: (800) 511-MSDS

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Hydrazine-History of the TLV/PEL

Year	TLV Standard
1956-1962	TLV-TWA = 1 ppm
1961-Present	Skin notation added (Systemic effects seen in animals following dermal contact)
1963	TLV-Ceiling = 1 ppm
1964-1976	TLV-TWA = 1 ppm
1975	TLV-TWA = 0.1 ppm, A2-suspected human carcinogen (Proposed-cancer, liver & blood effects)
1976	TLV-STEL = 0.3 ppm (Proposed)
1977	TLV-STEL proposal deleted (Insufficient IH & toxicology information to establish a STEL)
1977-1993	TLV-TWA = 0.1 ppm, A2-suspected human carcinogen (Pulmonary tumors in animals observed)
1989	TLV-TWA = 0.01 ppm (Proposed-Based on the slightly higher incidence of nasal tumors in rats)
1992	Documentation of the TLV revised
1993-Present	TLV-TWA = 0.01 ppm, A3-animal carcinogen

Carcinogenic Classification

ACGIH-TLV	A2-suspected human carcinogen (1977-1993), A3-animal carcinogen (1993-Present)
IARC	Group 2B-possibly carcinogenic to humans
NIOSH	Carcinogen-with no further classification
NTP	Group 2-reasonably anticipated to be a carcinogen
MAK	Group A2-carcinogenic in animal experimentation (Germany)

Other Nations

Australia	0.1 ppm, Category 2-probable human carcinogen, skin (1990)
Germany	0.1 ppm, Group A2-carcinogenic in animal experimentation, skin, sensitizer (1991)
Sweden	0.1 ppm, 0.3 ppm (STEL), carcinogenic, skin, sensitizer (1989)
UK	0.1 ppm, skin (1991)

Reference: ACGIH Documentation of the Threshold Limit Values (TLV's), 1992

Hydrazine Compound	Cal/OSHA PEL	Fed/OSHA PEL (Proposed-1989)
Hydrazine	TWA = 0.1 ppm	TWA = 1 ppm (TWA = 0.1 ppm)
Monomethylhydrazine (MMH)	Ceiling = 0.2 ppm	Ceiling = 0.2 ppm
1,1-Dimethylhydrazine (DMH)	TWA = 0.5 ppm	TWA = 0.5 ppm
Phenylhydrazine	TWA = 5 ppm, STEL = 10 ppm	TWA = 5 ppm (STEL = 10 ppm)
(Note: All have Skin notation)		

References: Cal/OSHA Section 5155, and Fed/OSHA Section 1910.1000

Other Standards

NIOSH REL-Ceiling = 0.03 ppm
NIOSH REL-IDLH = 80 ppm

Comments Regarding ACGIH TLV's

Since the mid-1950's, the ACGIH TLV-TWA has been lowered by a factor of 100 (from 1 ppm to 0.01 ppm). It is interesting to note that the ACGIH made two contradictory changes in the early 1990's. At the same time that they lowered the TLV-TWA from 0.1 ppm to 0.01 ppm (a tenfold decrease) based on the slightly higher incidence of nasal tumors in rats, they lowered the carcinogenicity category from A2 to A3 (as defined below).

A2-Suspected Human Carcinogen: The agent is carcinogenic in experimental animals at dose levels, by route(s) of administration, at site(s), of histologic type(s), or by mechanism(s) that are considered relevant to worker exposure. Available epidemiologic studies are conflicting or insufficient to confirm an increased risk of cancer in exposed humans.

A3-Animal Carcinogen: The agent is carcinogenic in experimental animals at a relatively high dose, by route(s) of administration, at site(s), of histologic type(s), or by mechanism(s) that are not considered relevant to worker exposure. Available epidemiologic studies do not confirm an increased risk of cancer in exposed humans. Available evidence suggests that the agent is not likely to cause cancer in humans except under uncommon or unlikely routes or levels of exposure.

(Note: Differences in wording are underlined)

Comments Regarding OSHA PEL's

When the OSHA Act was passed in 1970, Fed/OSHA adopted the 1968 ACGIH TLV's and incorporated them into law as the OSHA PEL table. When Cal/OSHA was formed in 1973, it is assumed that they did the same thing. As a result, it is likely that their original standard (PEL) for hydrazine in the early 1970's was 1 ppm.

Fed/OSHA never adopted the Fed/OSHA PEL changes proposed in 1989, since they were overturned in court. However, Cal/OSHA went ahead and made these changes. This is the reason why the current Cal/OSHA PEL's for several hydrazine compounds are more stringent than the current Fed/OSHA PEL's.

Internal Letter

Rockwell International

Date . February 3, 1983

No .

TO: (Name, Organization, Interna Address)
F. B. Lary
D/596, 055-SS12

FROM: Name, Organization, Interna Address, Phone)
J. K. Kwan
D/551, 055-SS11

~~5723~~
5273.

Subject: . RESPIRATORY PROTECTIVE PROGRAM

Sections 5144 (c)¢(h) of the CAL/OSHA General Industry Safety Orders (see attachment) specify medical and training requirements pertaining to the use of respiratory protective equipment .

These requirements, which apply to all operations involving the use of respirators, will be incorporated into the affected sections of the Rocketdyne Field Laboratories Procedures.

To comply with the regulation, Health & Safety has established a certification program for the use of respiratory protective equipment. It includes a medical examination and a training session. Test Management can now submit names of affected employees to Health & Safety for scheduling.

JK. Kwan

J. K. Kwan, Health & Safety Specialist

JKK:bbs

cc: All Test Managers
R. J. Lodge

Plan: 2/7/83.:

1. Lil collect names of all employees who may be reqd by their supervision to wear respirators, give list to Joe Kwan.
2. Joe will conduct training for all on the list (assuming the ones cleared for toxic have not had training)
3. Joe will arrange with medical for those on the list who have not had physical for toxics to have a physical for respirators. this may be special transport to Canoga medical + back
4. Follow up Mar 1.

2 - [illegible]
2 - [illegible]

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(A) The gas must be nontoxic and have a distinctive and strong enough odor to warn workmen of its presence if unburned.

(B) The maximum rate of gas supply to the make-up air heater shall not yield in excess of 2000 ppm of total combustible gas in the mixture upon flame failure.

(C) A fan shall be provided to remove the mixture of heated air and combustion products from gas burner plenum chambers. (Title 24, T8-5143)

NOTE: Authority cited: Section 142.3, Labor Code. Reference: Section 142.3, Labor Code.

HISTORY:

1. Amendment filed 7-16-76; effective thirtieth day thereafter (Register 76, No. 29)
2. Amendment of subsection (a) (2) filed 2-20-80; effective thirtieth day thereafter (Register 80, No. 8).

5144. Respiratory Protective Equipment.

(a) When and Where To Be Worn. When it is clearly impracticable to remove harmful dusts, fumes, mists, vapors, or gases at their source, as required in Sections 5141 and 5143 or where emergency protection against occasional and/or relatively brief exposure is needed, the employer shall provide, and the employee exposed to such hazard shall use, approved respiratory equipment.

(b) Approved Equipment. Whenever respirators are required to be used to control harmful exposures, only respiratory equipment approved for that purpose shall be used and such equipment shall be approved by the Mining Enforcement and Safety Administration or the National Institute for Occupational Safety and Health, Department of Health, Education, and Welfare. Only parts approved for the specific respirator system shall be used for replacement. Approval of equipment for which the above agencies have not established standards shall be contingent upon proof of its merits satisfactory to the Division. (See Section 3206).

(c) Education and Training. Employees shall be instructed and trained in the need, use, sanitary care, and limitations of such respiratory equipment as any employee may have the occasion to use. Respirators shall be inspected before each use and shall not be worn when conditions prevent a good gas-tight face seal. Every respirator wearer shall be instructed in how to properly fit and test respiratory equipment and how to check the facepiece fit and shall be provided the opportunity to wear respiratory equipment in normal air for an adequate familiarity period, and to wear it in a test atmosphere (such as generated by smoke tubes or isoamyl acetate).

(d) Maintenance and Sanitation.

(1) The employer shall provide, repair, or replace respiratory protective equipment as may be required due to wear and deterioration.

(2) Respirators maintained for emergency use shall be inspected and sanitized after each use and inspected at least monthly. A record of the most recent inspection shall be maintained on the respirator or its storage container, and shall include the inspector's identification, the date and a respirator identification number.

(3) The employer shall provide means for cleaning all respiratory protective equipment. Routinely used respiratory equipment shall be regularly cleaned, inspected, and sanitized by a qualified individual. Respiratory equipment shall not be passed on from one person to another until it has been cleaned and sanitized.

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(g) **Atmospheres Immediately Hazardous to Life or Health.** In atmospheres immediately hazardous to life or health, at least two persons equipped with approved respiratory equipment shall be on the job. Communications shall be maintained between both or all individuals present. Standby persons, at least one of which shall be in a location which will not be affected by any likely incidents, shall be present with suitable rescue equipment including self-contained breathing apparatus.

(h) **Medical Limitations.** Persons should not be assigned to tasks requiring use of respirators unless it has been determined that they are physically able to perform the work while using the required respiratory equipment. A licensed physician shall determine what health and physical conditions are pertinent. The medical status of persons assigned use of respiratory equipment should be reviewed at least annually. Wearing of contact lenses shall not be permitted in an atmosphere where a respirator is required.

(i) **Labeling Gas Mask Canisters.** Gas mask canisters shall be labeled and color coded as indicated in Table 1 before they are placed in service. The canister label shall include the following information:

In bold letters

(1) "Canister for _____"
(Name for Atmospheric Contaminant)
or
"Type N Gas Mask Canister"

(2) "For Respiratory Protection in Atmospheres Containing Not More Than ___ Percent by Volume of _____"
(Name of Contaminant)

Each canister shall have a label warning that gas masks should be used only in atmospheres containing sufficient oxygen to support life. Canisters having a special high-efficiency filter for protection against radionuclides and other highly toxic particulates shall be labeled with a statement of the type and degree of protection afforded by the filter.

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14 FEBRUARY 1983

D/598-346 - REQUIREMENTS FOR

RESPIRATORY PHYSICALS

W. COKER - HAS HAD ONE WITHIN THE LAST YEAR

M. GRANDCOLAS

E. LOCKWOOD

R. METZNER - HAS HAD ONE WITHIN THE LAST YEAR

F. PATOTA

J. PULTE

D. TYKER

BNA08768302

HDMSP001793989

11 February 1983

D/598-345

RESPIRATORY PROTECTIVE PROGRAM

PRIORITY

ALFA - R. M. BANAGA - 1
D. LOMBARDO - 1
G. W. MIRES - 2
W. E. GARRARD - 2

COCA 1ST - R. W. WILLIAMS - 1
D. R. ROACHE - 1
G. R. ALLSHOUSE - 2
T. A. PORTER - 2

COCA 2nd - J. J. MARTINEZ - 1
J. W. DODGE - 1
D. C. RODRIGUEZ - 1
N. E. BELL - 2

COCA 3rd - C. R. RINTOUL - 1
R. A. AABERG - 1
A. INGRASSI JR. - 2
C. C. BLUE - 2

BNA08768303

HDMSP001793990

11 February 1983

D/598-345

RESPIRATORY PROTECTIVE PROGRAM

PRIORITY

ALFA - R. M. BANAGA - 1
D. LOMBARDO - 1
G. W. MIRES - 2
W. E. GARRARD - 2

COCA 1ST - R. W. WILLIAMS - 1
D. R. ROACHE - 1
G. R. ALLSHOUSE - 2
T. A. PORTER - 2

COCA 2nd - J. J. MARTINEZ - 1
J. W. DODGE - 1
D. C. RODRIGUEZ - 1
N. E. BELL - 2

COCA 3rd - C. R. RINTOUL - 1
R. A. AABERG - 1
A. INGRASSI JR. - 2
C. C. BLUE - 2

BNA08768304

HDMSP001793991

14 FEBRUARY 1983

D/598-346 - REQUIREMENTS FOR

RESPIRATORY PHYSICALS

W. COKER - HAS HAD ONE WITHIN THE LAST YEAR

M. GRADCOLAS

E. LOCKWOOD

R. METZNER - HAS HAD ONE WITHIN THE LAST YEAR

F. PATOTA

J. PULTE

D. TYKER

BNA08768305

HDMSP001793992

412/273-5146

August 27, 1982

Mr. R. D. Bush
Rockwell International
6633 Canoga Avenue
Canoga Park, CA 91304

Dear Mr. Bush:

Enclosed you will find a copy of our test report on the M26A1 Gas Mask Canister. This is the same as our GMC-SSW Gas Mask Canister. As you will see, there is information contained in this report concerning service life of the canister against hydrazine, monomethylhydrazine, unsymmetrical dimethylhydrazine and red fuming nitric acid. All tests show an adequate service life against concentrations of these substances. We have no data concerning service life of the GMC-SSW Canister against nitrogen trioxide. We do feel, though, that the canister would be effective against this substance. If you have any further questions or need for further information concerning any of these substances, please do not hesitate to give us a call at the above number.

Sincerely,

R. D. Grunberg
Product Line Manager
Gas Masks and Respirators

elp

Enclosure

BNA08768306

Report No.: 81-23
TM81-5632
Job No.: A-2991
August 18, 1981

VALIDATION TESTING OF THE M26A1 GAS MASK CANISTER

BY

CHARLES C. ROBERTS

CONTRACT F09603-C-1716
DI-T-3714A
DI-T-3718A

MINE SAFETY APPLIANCES COMPANY
Research and Engineering Division
Pittsburgh, Pennsylvania

BNA08768307

HDMSP001793994

Report No.: 81-23
TM81-5632
Job No.: A-2991
August 18, 1981
Page 1

MINE SAFETY APPLIANCES COMPANY
Research and Engineering Division
Pittsburgh, Pennsylvania

VALIDATION TESTING OF THE M26A1 GAS MASK CANISTER

By

Charles C. Roberts

Part 1. Validation Testing of the M26A1 Gas Mask Canister

1. Introduction

This investigation was carried out for the purpose of determining the effectiveness of the M26A1 Gas Mask Canister for preventing passage of hydrazine, monomethyl hydrazine, unsymmetrical dimethyl hydrazine, Aerozine 50, and red fuming nitric acid at less than the Threshold Limit Value concentration of the propellants. Originally, it was intended to use specific (colorimetric) tests for measuring leakage of these materials. This turned out to be impossible because the propellants all undergo chemical reaction while passing through the canister and the penetrating gases are not hydrazines, but rather ammonia and/or amines. (The same observation applies to RFNA; the penetrating gas is not NO_2 or HNO_3, but nitric oxide, NO.)

This report consists of four parts:

Part 1. A general discussion of methods and results.
Part 2. A recommended Acceptance Test for the canister.
Part 3. A table of test results.
Part 4. An appendix which discusses some of the analytical methods in detail.

The recommended acceptance test procedure tests the canister against hydrazine, unsymmetrical dimethyl hydrazine (UDMH), and red fuming nitric acid (FRNA), but not against monomethyl hydrazine.

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HDMSP001793995

2. Test Results

2.1 Original Objective

2.1.1 Determine performance of canister against UDMH: end point 0.5 ppm determined by trisodium pentacyanoamino ferroate (TPF) method.

2.1.2 Determine performance of canister against hydrazine: end point 0.1 ppm determined by p-dimethylaminobenzaldehyde (PDAB) method.

2.1.3 Determine performance of canister against methylhydrazine: end point 0.2 ppm determined by PDAB method.

2.1.4 Determine performance against mixture of UDMH and hydrazine: end points to be determined as above.

2.1.5 Determine performance of canister against Red Fuming Nitric Acid (RFNA): end point 3 ppm (as NO_2).

2.2 Description of Canister

The contents of the Rocket Propellant Canister M15A1 (MSA Type GMN-SSW) are from bottom to top:

2.2.1 High efficiency filter
2.2.2 Soda lime
2.2.3 Silica gel
2.2.4 Indicating Window
2.2.5 Activated Carbon

An indicating window is positioned at the silica gel layer. The indicator is a chromic acid impregnated silica gel which responds to reducing agents such as 1,1 dimethyl hydrazine. The canister is recommended for use against red fuming nitric acid, nitrogen tetroxide, unsymmetrical dimethyl hydrazine, hydrazine, hydrogen peroxide, and organic vapors such as kerosene, aniline, and alcohol.

The window indicator applies only to protection afforded against red fuming nitric acid and unsymmetrical dimethyl hydrazine. Even here, it is not effective against RFNA under all conditions. In fact, the window indicator may be misleading and should not be relied upon except with UDMH!

2.3 Analytical Methods

The TPF and PDAB methods were calibrated using stock solutions containing 0.05 ml of the hydrazines per liter. Calibration curves so obtained indicated adequate sensitivity: 0.004 ppm (gas) in 10 liters for hydrazine, 0.16 ppm (gas) in 10 liters for UDMH and 0.2 ppm (gas) in 20 liters for MMH. However, these methods were quite slow (1 to 4 hours for color development) so a faster method, using the reaction of hydrazines with iodine, was devised.

The iodine method made use of the reaction $I_2 \xrightarrow{\text{hydrazines}} 2I^-$

The resulting iodide was analyzed by means of an iodide selective-ion electrode using the known addition method of analysis. This method was found to be capable of analyzing hydrazines at the required low level and was not as time consuming as the colorimetric methods. However, it obviously cannot distinguish between various hydrazines.

For a given volume of gas, the iodine method was generally more sensitive than the color methods; it is capable of detecting concentrations of 0.03 - 0.06 ppm in a 10 liter sample.

2.4 Analytical Results

Neither the iodine method nor the colorimetric methods could detect any trace of hydrazines in the effluent gas from canisters during gas testing. No hydrazines were detected even long after some unknown gas had broken through the canister as shown by smell, window indication, instrumental detection, or acid-base indicator papers. It appears that the hydrazines undergo reactions in the canister and some other gas or gases appear in the canister effluent.

For example, with hydrazine (N_2H_4) itself, the canister becomes warm at the bottom, in the soda lime layer, and the window never changes. Apparently some reaction such as $N_2H_4 \xrightarrow{O_2} N_2 + 2H_2O$ and/or $3N_2H_4 \rightarrow N_2 + 4NH_3$ occurs in the soda lime layer. These reactions indicate that the penetrating gas may well be ammonia and would explain the lack of window indication.

2.5 Instrumental End Point Detection

Because the penetrating gases are not hydrazines, it was determined that a general instrumental detection system to detect various compounds containing nitrogen might be more appropriate for end point detection during hydrazine tests. It was found that a photoionization gas analyzer is adequate. This device is sensitive to hydrazines and also to many of the possible reaction products produced within the canister, primarily amines and ammonia.

In running a given gas test, the procedure was to calibrate the instrument against the appropriate hydrazine and then to assume that the penetrating gas was the same as the challenge gas.

In practical terms this means running the instrument at its highest sensitivity and then taking any response (a few scale divisions) as the end point of the test.

This is a reasonably "fail-safe" approach in that the effluent gases, in general, are much less toxic than hydrazines; therefore, the instrument end point is reached well before the effluent becomes hazardous.

This appraoch was successful with hydrazine and 1,1 dimethyl hydrazine; however, with monomethyl hydrazine it gives somewhat misleading results, as will be discussed below.

2.6 Test Results

Test results for unsymmetrical dimethyl hydrazine, hydrazine, hydrazine plus dimethyl hydrazine, monomethyl hydrazine, and red fuming nitric acid are shown in Table 1, part 3.

The service times in all of these tests are adequate, ranging from 17 minutes (UDMH, at 2% concentration) to 180 minutes, (hydrazine, equilibrated at 85% RH and tested at 0.5% concentration). The canister is capable of scrubbing all of these contaminants from an air stream at fairly high concentrations for a reasonable period of time. Results of these various tests are discussed in some detail below.

2.6.1 UDMH: No UDMH was found in the canister effluent by either the colorimetric (TPF) or iodine method, even at twice the canister's service time (as indicated instrumentally). The canister does not become hot at the soda lime layer; it appears that the silica gel (and carbon) layers adsorb the UDMH. The lack of UDMH in the effluent may be explained by some reaction such as: $3H_2NN(CH_3)_2 \longrightarrow N_2 + 2NH_3 + 2(CH_3)_3N$ and/or $3H_2NN(CH_3)_2 \longrightarrow N_2 + 2CH_3NH_2 + 2(CH_3)_2NH$, the net result being ammonia plus an amine. The likely penetrating gas in this case would be ammonia; the amines would be adsorbed on the carbon more effectively than the ammonia.

The window indication is quite distinct with UDMH and occurs when the canister is about 40-60% expended.

2.6.2 Hydrazine

The canister's service time against hydrazine is greater than 100 minutes at 0.50% concentration and 32 lpm. However, there is no window change during the course of the test.

The warm zone in the canister is in the soda-lime layer rather than the silica gel layer as one might expect. Some reaction such as: $N_2H_4 \xrightarrow{O_2} N_2 + H_2O$ and/or $3N_2H_4 \longrightarrow N_2 + 4NH_3$ apparently occurs in the soda lime layer; thus, no hydrazine gets to the window indicator and no color change occurs. From the above equations it would appear that the penetrating gas is ammonia.

2.6.3 UDMH + Hydrazine

Mixed tests were run with 1.0% UDMH and 0.5% hydrazine. With this mixture the canister performed as if it were tested against 1.5% UDMH. (With 2% UDMH, the canister lasted about 20 minutes; with 1% UDMH, one would expect about 40 minutes. With the mixture, the canister lasted about 30 minutes.) The window indicator performed adequately showing distinct indication at about 50 - 70% of the service time.

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In the event of a spill of a 50-50 mixture of UDMH and hydrazine one would expect the UDMH vapor to be present at a concentration of about 10 times that of the hydrazine. (UDMH vapor pressure at 25°C -157.3 mm Hg, hydrazine vapor pressure at 25°C ~ 14.2 mm Hg.) Therefore, the service time of the canister would be determined mostly by the UDMH vapor, the window would give adequate warning, and the canister would be suitable for such service.

2.6.4 Monomethyl Hydrazine (MMH)

The photoionization detection system was not completely satisfactory when used in MMH testing. A number of spurious "breaks" were recorded before the "real" break occurred. In Table 1 the number in parentheses are the initial break times. On further investigation it was found that:

A. An immediate large signal was recorded from the beginning of the test by a Total Hydrocarbons Analyzer.

B. Gas chromatographic analysis showed large quantities (~1000 ppm) of methane from the beginning of the test.

C. After 30-40 minutes testing, a gas chromatograph peak appeared which could be identified as methyl alcohol. (A third GC peak was present from early in the test, but it was not identified.)

These results indicate that two reactions occurring in the canister (at the soda lime layer, which gets warm) are $CH_3 NH NH_2 \xrightarrow{O_2} CH_4 + N_2 + H_2O$ and $CH_3 NH NH_2 \xrightarrow{O_2} N_2 + CH_3OH + H_2O$.

The first reaction is apparent from the very beginning of the test; the second one shows up after about one half hour.

At about 40 minutes, the photoionization detector shows a strong, sharply rising signal. This is the true end point of the test. Both the GC methyl alcohol peak and the Total Hydrocarbons analyzer also show some increase beginning at 40 minutes. This break is probably methyl alcohol plus ammonia penetrating the canister: $3 CH_3 NH NH_2 \longrightarrow N_2 + NH_3 + 3CH_3 NH_2$ and/or $3CH_3 NH NH_2 \longrightarrow N_2 + 3NH_3 + (CH_3)_3N$.

The window shows a reasonable correlation with the final break (40% - 70% indication); however, it is very late with respect to the first instrumental indication.

2.6.5 Red Fuming Nitric Acid

The service time of the canister against Red Fuming Nitric Acid (RFNA) at 1% concentration and 25 lpm is about 50 minutes in the as-received condition. This drops to 20-30 minutes upon equilibration at 85% RH and 25% RH. With the as-received cans the window indication was apparent at about 70% of the service time.

The equilibrated canisters showed no apparent window indication. This may be because the service time was relatively short (20-30 minutes). If this were the case, it is not a very hazardous situation because the breaking gas, NO, has a relatively high TLV (25 ppm). This, of course, assumes that the window does change not too long after NO leakage begins.

2.6.7 Summary

2.6.7.1 The hydrazines are quite unstable; therefore, the gases penetrating the canister are not hydrazines, but rather various reaction products of hydrazines such as ammonia, amines, methane, methyl alcohol, etc. As far as use of the canister is concerned, this is not an undesirable situation because the reaction products are much less toxic than the hydrazines.

2.6.7.2 The service time of the canister is adequate; for concentrations in the 0.5-2.0% range it should provide protection for at least 20-30 minutes. The penetrating gas is usually ammonia, which can be readily detected by odor.

2.6.7.3 The window indicator is adequate for indicating approaching canister exhaustion for 1,1 dimethyl hydrazine, 1,1 dimethyl hydrazine + hydrazine (at least under the expected conditions where such a mixture might occur), monomethyl hydrazine, and RFNA in the as-received condition. The window shows no indication with hydrazine alone and its behavior in equilibrated RFNA tests is questionable.

Part 2. Acceptance Test Procedures

3. Suggested Acceptance Test for Rocket Fuel Canister

It is recommended that the Acceptance Test Procedure for the canister use hydrazine, UDMH and RFNA. The hydrazine will test the soda lime layer to see that it is performing properly, while the UDMH will challenge the silica gel and carbon layers. RFNA, being a completely different chemical species, must be tested separately. Monomethyl hydrazine should not be used as an acceptance test gas because of its odd response, due to decomposition products, on the photoionization instrumentation. Further, if the canister performs satisfactorily against hydrazine and UDMH, it will work against MMH.

3.1 Objective

3.1.1 To ensure that the canister will provide protection when used against hydrazines and red fuming nitric acid.

3.2 1,1 dimethyl hydrazine (UDMH)

3.2.1 Description of Test

3.2.1.1 The canister is tested against 2% UDMH at 32 lpm to an end point corresponding to a leakage of 0.5 ppm UDMH.

3.2.2 End Point Detection

3.2.2.1 An HNU Continuous Gas Monitor (a photoionization instrument) is used at maximum sensitivity for end point determination.

3.2.2.2 Calibration of photoionization instrument.

3.2.2.2.1 Materials

3.2.2.2.1.1 75 liter gas bag.

3.2.2.2.1.2 10 cc gas syringe

3.2.2.2.1.3 Trisodium pentacyanoamino ferrate (TPF color reagent), 0.1% solution in deionized water.

3.2.2.2.1.4 Buffer solution, Ph 5.4; 5.65 g disodium acid phosphate ($Na_2 HPO_4 7H_2O$) and 1.92 g citric acid dissolved in 2 liters deionized water.

3.2.2.2.1.5 UDMH standard solution: 0.05 ml (0.0393 g) dissolved in 1 liter deionized water. Contains 39.3 mg UDMH/ml.

3.2.2.2.1.6 Plastic bubblers

3.2.2.2.1.7 Test tubes (~35 ml capacity)

3.2.2.2.1.8 Spectrophotometer with cuvettes.

3.2.2.2.1.9 Pump and flow meter for 1 lpm flow.

3.2.2.2.1.10 UDMH

3.2.2.2.2 Procedure

3.2.2.2.2.1 Make a bag mix of about 10 ppm UDMH; about 4 cc saturated UDMH vapor in 75 liters air.

3.2.2.2.2.2 Determine instrument response to bag mix. Should be on the X10 scale.

3.2.2.2.2.3 Analyze bag mix by TPF method.

3.2.2.2.2.3.1 Prepare standard solution: 2, 4, 6, and 8 ml of UDMH standard solution made up to 20 ml with buffer solution.

3.2.2.2.2.3.2 Collect gas sample: 10 liter samples pulled through plastic bubblers containing 20 ml buffer solution.

3.2.2.2.2.3.3 10 ml of each of the standards and 10 ml of solution from the gas bubblers are then treated with 1 ml of TPF reagent. The samples are allowed to stand for 1 hour, then are read on the spectrophotometer at 500 mμ. A plot of A vs. μg UDMH is constructed from the standards data; the amount of UDMH in the gas sample is read from the standard curve and the gas concentration is calculated from $C(ppm, gas) = \frac{\mu g\ (UDMH)}{V \cdot 2.45}$, where V is the gas volume (liter).

3.2.2.3 Calculations

From 3.2.2.2.2.2 and 3.2.2.2.2.3.3, obtain the gas concentration and the number of divisions obtained on the photoionization instrument. Then response = $\frac{\text{scale divisions}}{\text{ppm}}$. For example, 12 ppm and 120 divisions (12 on X10 scale) are obtained and response = $\frac{120\ \text{div}}{12\ \text{ppm}}$ = 10 div/ppm. As the desired end point is 0.5 ppm, the instrument end point is 0.5 ppm x 10 $\frac{\text{div}}{\text{ppm}}$ = 5 divisions.

3.2.2 Gas Test

3.2.3.1 Test System

(Block diagram shown in Figure 1).

3.2.3.1.1 The test system is a conventional gas test apparatus. The UDMH is supplied by bubbling nitrogen through UDMH.

3.2.3.1.2 Components

3.2.3.1.2.1 Compressed air supply

3.2.3.1.2.2 Compressed air filter

3.2.3.1.2.3 Humidifier

3.2.3.1.2.4 Humidity sensor

3.2.3.1.2.5 Nitrogen supply

3.2.3.1.2.5 Flow meter (nitrogen)

3.2.3.1.2.6 UDMH bubbler (~ 4 liter bottle)

3.2.3.1.2.7 Test fixture for holding canister

3.2.3.1.2.8 Flow meter (canister flow)

3.2.3.1.2.9 Leak detection system (see 2.2).

3.2.3.1.2.10 Balance, 2 kg capacity capable of weighing to 0.1 g.

3.2.3.1.3 Operation

The UDMH concentration is calculated from the weight loss of the UDMH bubbler (for a concentration of 2% at 32 lpm, the weight loss is 1.57 g/min.).

3.2.3.1.3.2 The air flow and nitrogen flow are adjusted to give a) 32 lpm measured with the canister flow meter and b) 2.0% UDMH as measured by the bubbler weight loss.

3.2.3.1.3.2 The nitrogen flow should be about 2 lpm.

3.2.3.1.3.3 The test is run on an as-received canister at 50% RH.

3.2.3.1.3.4 The test is run to an indicated leakage of 0.5 ppm UDMH as described in 3.2.2.

3.2.3.2 Required Performance

3.2.3.2.1 The service time to an indicated leakage of 0.5 ppm UDMH shall be no less than 10 minutes.

3.2.3.2.2 If a windowcator is used, it shall show definite evidence of change at 30-80% of the service time.

3.3 Hydrazine

3.3.1 Description of Test

3.3.1.1 The canister is tested against 0.5% hydrazine to an end point corresponding to a leakage of 0.1 ppm hydrazine.

3.3.2 End Point Detection

3.3.2.1 An HNU Continuous Gas Monitor (a photoionization instrument) is used at maximum sensitivity for end point determination.

3.3.2.2 Calibration of photoionization instrument.

3.3.2.2.1 Materials

3.3.2.2.1.1 75 liter gas bag.

3.3.2.2.1.2 10 cc gas syringe

3.3.2.2.1.3 p-dimethylamino benzaldehyde (DMBA color reagent), 2.5% solution in methanol.

3.3.2.2.1.4 Glacial acetic acid

3.3.2.2.1.5 Hydrazine standard solution: 0.05 ml dissolved in 1 liter deionized water. Contains 0.050 mg hydrazine per ml.

3.3.2.2.1.6 Plastic bubblers.

3.3.2.2.1.7 Test tubes (~ 35 ml capacity).

3.3.2.2.1.8 Spectrophotometer with cuvettes.

3.3.2.2.1.9 Pump and flow meter for 1 lpm flow.

3.3.2.2.1.10 Hydrazine (anhydrous).

3.3.2.2.2 Procedure

3.3.2.2.2.1 Make a bag mix of 1-2 ppm hydrazine: 10 cc saturated vapor in a 75 liter bag.

3.3.2.2.2.2 Determine instrument response to bag mix.

3.3.2.2.2.3 Analyze bag mix by DMBA method.

3.3.2.2.2.3.1 Prepare standard solutions: 0.05, 0.10, 0.20, and 0.40 ml of hydrazine standard made up to 20 ml with deionized water.

3.3.2.2.2.3.2 Collect gas sample: 10 liter sample pulled through plastic bubbler containing 20 ml deionized water.

3.3.2.2.2.3.3 10 ml of each of the standard and 10 ml of solution from the gas bubbler are then treated with 10 ml of DMBA solution. The samples are allowed to stand for four hours and are then treated with 10 ml glacial acetic acid. The samples are then allowed to stand for 15-20 minutes and are then read on the spectrophotometer at 480 mμ. A plot of A vs. μg of hydrazine is then constructed from the standards data; the amount of hydrazine in the gas sample is read from the calibration curve and the gas concentration is calculated from $C(\text{ppm, gas}) = \frac{\mu g \text{ (hydrazine)}}{V \cdot 1.31}$, where V is the gas volume (liters).

3.3.2.2.3 Calculations

From 3.3.2.2.2.2 and 3.3.2.2.2.3.3, obtain the gas concentration and the number of divisions obtained on the photoionization instrument. Then response $= \frac{\text{scale divisions}}{\text{ppm}}$. For example, 40 divisions and 1.4 ppm are obtained so response $= \frac{40 \text{ div}}{1.4 \text{ ppm}} = 29 \text{ div/ppm}$. As the desired end point is 0.1 ppm, the instrument end point is 0.1 ppm x $\frac{29 \text{ div}}{\text{ppm}}$ or about 3 divisions.

3.3.3 Gas Test

3.3.3.1 Test System

(Block diagram shown in Figure 2).

3.3.3.1.1 The test system is a conventional gas test apparatus. The hydrazine is supplied by bubbling a portion of the main air flow through hydrazine.

3.3.3.1.2 Components

3.3.3.1.2.1 Compressed air supply.

3.3.3.1.2.2 Compressed air filter.

3.3.3.1.2.3 Humidifier.

3.3.3.1.2.4 Humidity sensor.

3.3.3.1.2.5 Hydrazine bubbler (~4 liter bottle)

3.3.3.1.2.6 Test fixture for holding canister.

3.3.3.1.2.7 Flow meter

3.3.3.1.2.8 Leak detection system

3.3.3.1.2.9 Balance, 2 kg capacity capable of weighing to 0.1 g.

3.3.3.1.3 Operation

3.3.3.1.3.1 The hydrazine concentration is calculated from the weight loss of the hydrazine bubbler (for a concentration of 0.5% at 32 lpm, the weight loss is 0.21 g/min.).

3.3.3.1.3.2 The air flow and by-pass flow are adjusted to give a) 32 lpm total flow and b) 0.5% hydrazine as measured by the bubbler weight loss.

3.3.3.1.3.3 The test is run on an as-received canister; the humidity is essentially that of compressor air (no water added).

3.3.3.1.3.4 The test is run to an indicated leakage of 0.1 ppm hydrazine as described in 3.3.2.

3.3.3.2 Required Performance

3.3.3.2.1 The service time to an indicated leakage of 0.1 ppm hydrazine shall be no less than 75 minutes.

3.4 Red Fuming Nitric Acid (RFNA)

3.4.1 Description of Test

3.4.1.1 The canister is tested against RFNA at a concentration of 1.0% (as HNO_3) at 32 lpm, to a leakage of 0.30 ppm (as NO_2).

3.4.2 End Point Detection

3.4.2.1 A wet chemical method, sensitive to oxides of nitrogen (NO and NO_2) with KI-starch as the detection medium is used.

3.4.2.2 Description

1/2 liter per minute of the effluent is directed through three bubblers in series: 1) a bubbler containing 30 ml concentrated sulfuric acid; 2) a bubbler containing 30 ml potassium permanganate; and 3) a bubbler containing 25 ml 10% potassium iodide solution plus 5 ml 0.1% starch solution. A change of the starch-iodide bubbler to bluish-brown within 5 minutes constitutes the end of the test.

3.4.2.3 Calculation of sensitivity of the method

3.4.2.3.1 Assumptions

3.4.2.3.1.1 The gas penetrating the canister is NO.

3.4.2.3.1.2 The sensitivity of starch-iodide solution is 10^{-6}N.

3.4.2.3.1.3 The reactions involved are: $5NO + 2KMnO_4 + 3H_2SO_4 \longrightarrow 5NO_2 + 2MnSO_4 + K_2SO_4 + 3H_2O$ and $NO_2 + 2HI \rightarrow I_2 + H_2O + NO$. From these it appears that 1 equivalent of NO produces 1 equivalent of iodine.

3.4.2.3.2 Calculations

3.4.2.3.2.1 Equivalents required for bubbler change = 0.03 liter x 10^{-6} 10^{-6} equ/liter = 3×10^{-8} equivalents. Volume of NO required: $V = \frac{NRT}{P} = \frac{3 \times 10^{-8} \times 24.5}{1} = 7.35 \times 10^{-7}$ liters. This amount of NO is contained in a 2.5 liter sample of air. Therefore, conc. $= \frac{7.35 \times 10^{-7} \text{ liter NO}}{2.5 \text{ liter air}} = 2.94 \times 10^{-7}$ liter (NO)/liter (air) $\cong$ 0.3 ppm.

3.4.3 Gas Test*

3.4.3.1 Test System

(Block diagram shown in Figure 3).

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3.4.3.1.1 The test system is a conventional gas test apparatus. The RFNA is supplied via a heated vaporizer.

3.4.3.1.2 Components.

3.4.3.1.2.1 Compressed air supply.

3.4.3.1.2.2 Compressed air filter.

3.4.3.1.2.3 Humidifier.

3.4.3.1.2.3 Humidity sensor

3.4.3.1.2.4 Vaporizer

3.4.3.1.2.5 RFNA pump.

3.4.3.1.2.6 RFNA supply.

3.4.3.1.2.7 Test fixture (for canister).

3.4.3.1.2.8 Flow meter (canister flow).

3.4.3.1.2.9 Leak detection (see 3.2).

*The current test is conducted at 25 lpm, intermittent flow. It is suggested that this be changed to 32 lpm, constant flow.

3.4.3.1.3 Operation

3.4.3.1.3.1 Required RFNA flow is calculated from the density and composition of the liquid RFNA.

3.4.3.1.3.2 Air flow is 32 lpm.

3.4.3.1.3.2 The test is run on an as-received canister at 10% RH.

3.4.3.1.3.2 The test is run to an indicated leakage of 0.3 ppm as described in 3.4.2.

3.4.3.2 Required Performance

3.4.3.2.1 The service time to an indicated leakage of 0.3 ppm (as NO_2) shall be at least 10 minutes.

3.4.3.2.2 If a window indicator is used, it shall show definite evidence of change at 60-80% of the service time.

Part 3. Test Results

Table 1. Various test results on Type GMN-SSW canister.

AR: as-received
equ. 85%: equilibrated for 6 hours at 64 lpm and 85% RH.
equ. 25%: equilibrated for 6 hours at 64 lpm and 25% RH.
Test RH: 50%*
End point: First indication with HNU Photoionization Continuous Gas analyzer.

*Except for hydrazine; see 3.3.3.1.3.3.

UDMH: 2%, 32 lpm

	Service Time	Window Indication time	Window Indication %
AR	17 min.	8 min.	47
AR	22 min.	13 min.	59
equ. 85%	22 min.	7 min.	32
equ. 85%	27 min.	11 min.	41
equ. 25%	22 min.	10 min.	45
equ. 25%	19 min.	9 min.	47

H: 0.5%, 32 lpm

	Service Time	Window Indication
AR	107 min.	no window change
AR	131 min.	no window change
equ. 25%	95 min.	no window change
equ. 25%	114 min.	no window change
equ. 85%	170 min.	no window change
equ. 85%	180 min.	no window change

H + UDMH (0.5% + 1.0%)

	Service Time	Window Indication time	%
AR	24 min.	18 min.	75
AR	30 min.	19 min.	63
25% equ.	29 min.	18 min.	62
25% equ.	25 min.	13 min.	52
85% equ.	39 min.	12 min.	31
85% equ.	31 min.	15 min.	48

MMH: 1.0% 32 lpm
10×10^3 ppm

	Service Time	Window Indication time	%
AR	35-40 min. (7 min.)	20 min.	57
AR	40 min. (8 min.)	30 min.	75
25% equ.	40-45 min. (9 min.)	20 min.	50
25% equ.	40-45 min. (8 min.)	20 min.	50
85% equ.	40-45 min. (6 min.)	15 min.	38
85% equ.	40-45 min. (3 min.)	17 min.	42

RFNA: 1%, 25 lpm

	Service Time	Window Indication time	%
AR	54 min.	38 min.	70
AR	46 min.	32 min.	70
equ. 25%	32 min.	no definite change	
equ. 25%	27.5 min.	no definite change	
equ. 85%	23 min.	no definite change	
equ. 85%	20 min.	no definite change	

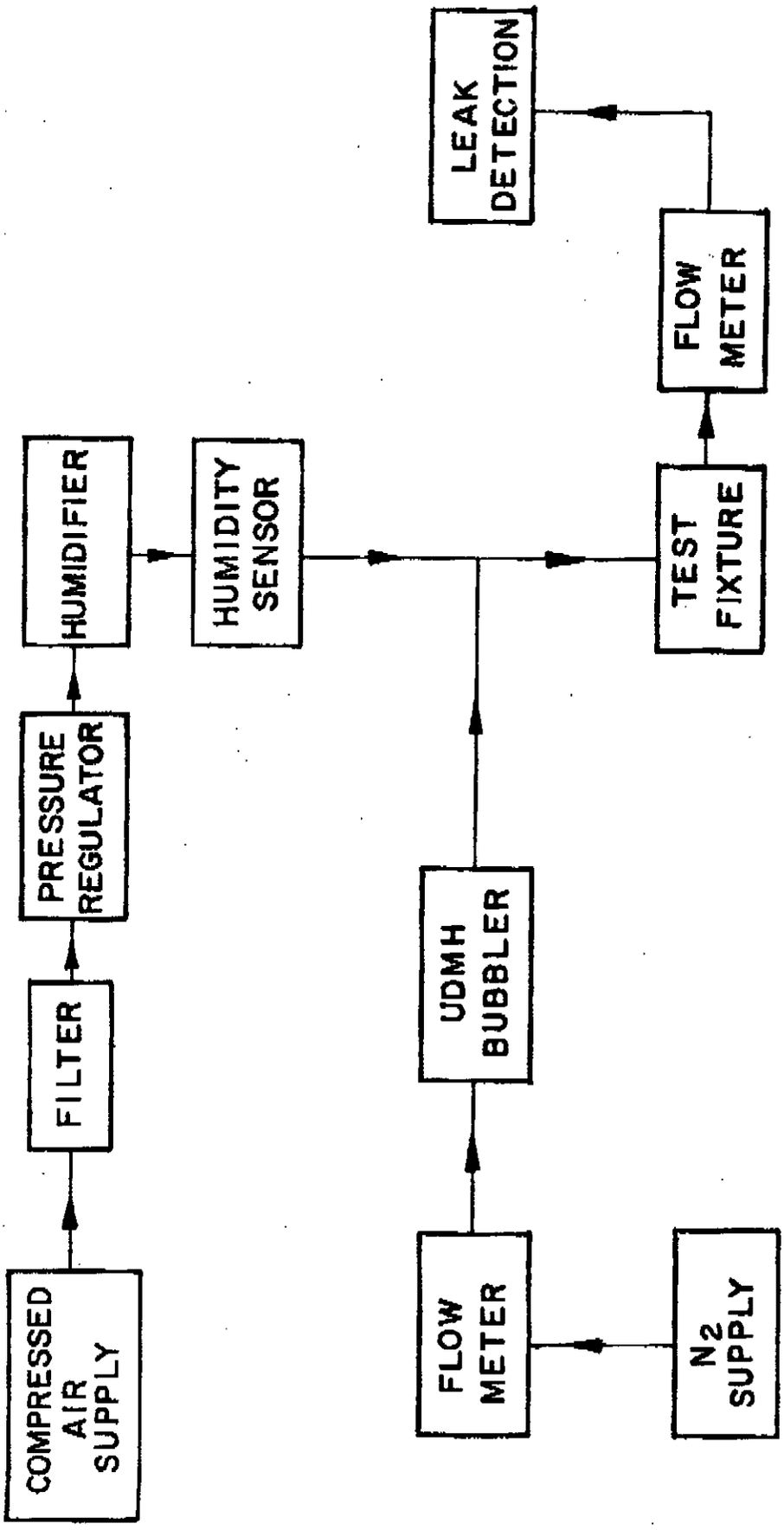

FIGURE I. UDMH TEST APPARATUS

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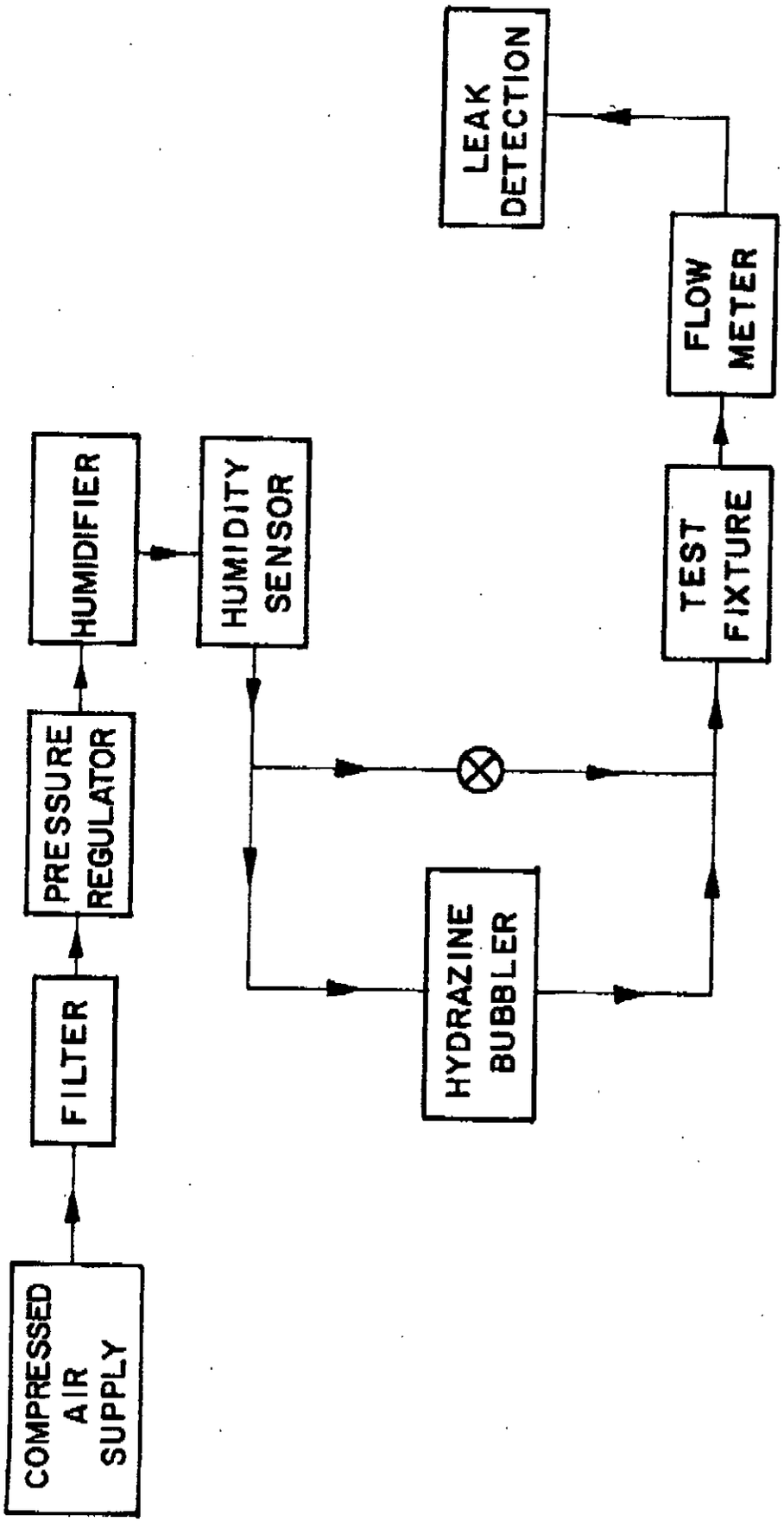

FIGURE 2. HYDRAZINE TEST APPARATUS

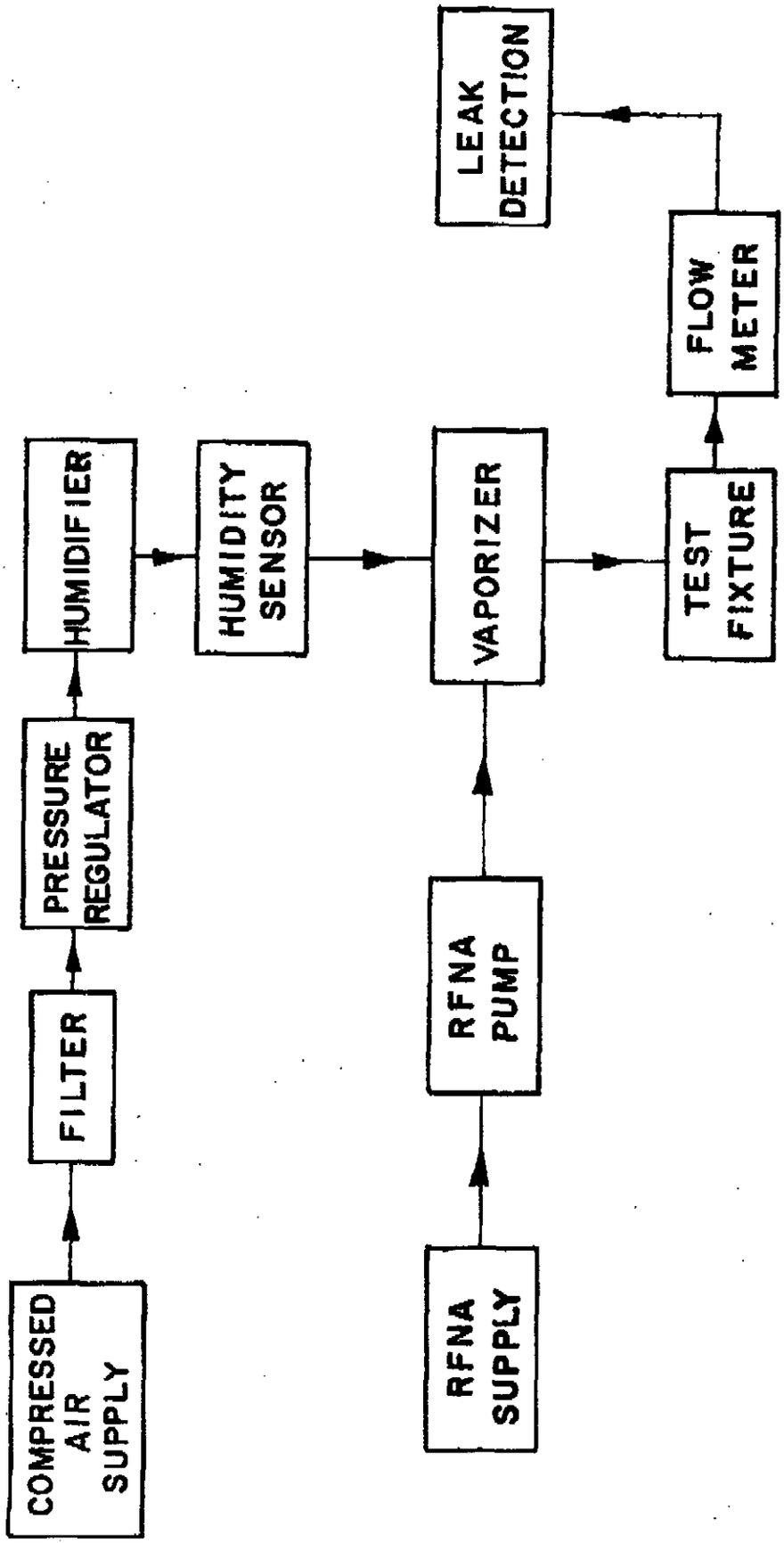

FIGURE 3. RFNA TEST APPARATUS

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Part 4. Appendix: Analytical Methods

4.1 Tri-sodium pentacyanoamino ferroate (TPF), colorimetric analysis for UDMH.

4.1.1 Reference: M. K. Pinkerton, J. M. Lauer, P. Diamond, and A. A. Tumas; "A Colorimetric Determination for 1,1 Dimethyl Hydrazine (UDMH) in Air, Blood and Water", Am. Ind. Hyg. Assoc. J. 24: 239-44, 1963.

4.1.2 Calibration

Given quantity of stock solution (0.05 cc UDMH/liter) made up to 20 ml with buffer solution. 10 ml of resulting solution treated with 1 ml of TPF solution (0.1% in deionized water). Samples allowed to stand one hour and then are read on the Spectronic 20 at 500 mμ. Blank (100% T) made with 10 ml buffer solution, 1 ml TPF solution.

For example:

Sample	μg UDMH / 20 ml	% T	A
blank	----	100	0
1 ml stock	39.3	59.5	0.225
4 ml stock	157	14.5	0.828

A is then plotted vs. μg UDMH to produce the calibration curve. (See Figure 4.)

4.1.3 Gas Samples

20 cc buffer solution in bubbler; 1 lpm, time t. Take 10 cc from bubbler and treat as above. μg UDMH determined from calibration curve. 1.0 ppm = 2.45 μg UDMH/liter; therefore: conc. (ppm, gas) = $\frac{\mu g \text{ UDMH}}{t \cdot 2.45}$. For example, 10 min. sample at 1 lpm with 20 μg UDMH would yield: conc. (ppm, gas) = $\frac{20}{10 \cdot 2.45}$ = 0.81 ppm.

4.2 Dimethylaminobenzaldehyde (DMBA), colorimetric analysis for hydrazine.

4.2.1 Reference: T. Dambraushas and H. H. Cornish; "A Modified Spectrophotometric Method For The Determination of Hydrazine", Am. Ind. Hyg. Assoc. J. 23:151-56, 1962.

4.2.2 Calibration

Given quantity of stock solution made up to 20 ml with deionized water. 10 ml of resulting solution treated with 10 ml of DMBA solution (2.5% in methanol). Let stand for four hours then add 10 ml glacial acetic acid. Wait 15-20 minutes then read on the Spectronic 20 at 480 mμ. Blank (100% T) made with 10 ml deionized water.

For example:

Sample	μg H / 20 ml	% T	A
Blank	----	100	0
0.05 ml stock	5	71	0.149
0.10 ml stock	10	52	0.284
0.20 ml stock	20	27	0.569

A is then plotted vs. μg hydrazine to obtain the calibration curve. (See Figure 5).

4.2.3 Gas Samples

20 ml deionized water in bubbler; 1 lpm, time t. Take 10 ml from bubbler and treat as above. μg hydrazine determined from calibration curve. For hydrazine: 1.0 ppm = 1.31 μg/liter; therefore: conc. (ppm, gas) = $\frac{\mu g\ H}{t \cdot 1.31}$

For example:

10 min. sample at 1 lpm with 5 μg hydrazine would yield: conc. (ppm, gas) = $\frac{5}{10 \cdot 1.31}$ = 0.38 ppm.

4.3 Dimethylaminobenzaldehyde (DMBA), colorimetric analysis for monomethyhydrazine.

4.3.1 The method is the same as that used for hydrazine except that it is less sensitive.

Example:

Sample	μg MMH / 20 ml	% T	A
Blank	------	100	0
1 ml stock	43.3	86.0	0.065
2 ml stock	86.6	65.0	0.187
4 ml stock	173	35.5	0.450
8 ml stock	346	16.0	0.796

4.3.2 Gas Samples

20 ml deionized water in bubbler; 1 lpm, time t. Take 10 ml from bubbler and treat as with hydrazine. µg monomethylhydrazine determined from calibration curve. (See Figure 6). For monomethyl hydrazine: 1.0 ppm = 1.88 µg/liter. Therefore, conc. (ppm, gas) = $\frac{\mu g/liter}{t \cdot 1.88}$. For example: 10 minute sample at 1 lpm with 20 µg MMH would yield: conc. (ppm, gas) = $\frac{20}{10 \cdot 1.88}$ = 1.06 ppm.

4.4 Iodine Method for Analysis of Hydrazines

The preceeding colorimetric methods are quite specific, but they are also slow (1-4 hours for color development). While running canister gas tests it is desirable to obtain leakage information while the test is in progress.

A method was devised which requires only a few minutes. It is not specific for each hydrazine, being based on the reaction of iodine with hydrazines, which produces iodide ions: iodine $\xrightarrow{\text{hydrazines}}$ iodide ions.

Under the conditions employed, the reaction is not quantitative; in terms of iodide ions produced per hydrazine molecule we obtained for

MMH: $3I^-$ per molecule
UDMH: $2I^-$ per molecule
H: 2.7 I^- per molecule

4.4.1 The procedure was as follows:

To 20 ml of the hydrazine solution add 2 ml 0.1 N H_2SO_4 (to repress the reaction $3I_2 + 6OH^- \longrightarrow IO_3^- + 5I^-$) and 2 ml of deionized water saturated with iodine. The solution is then diluted to 50 ml.

The iodide electrode and reference electrode are placed in the solution. The meter needle is set to ∞ on the known addition scale (meter in the log anion mode). Then 0.05 ml of 0.01 N KI are added, with stirring, and the new position of the needle is noted.

The concentration of the unknown solution is then given by: concentration = ΔC x meter reading, where $\Delta C = \frac{0.05 \times 0.01}{50 + 0.05} \cong 1. \times 10^{-5} N$. (It is also necessary to take a blank reading in order to cancel out any other sources of iodide ion.)

For example, with UDMH, three samples containing 1.79 µg UDMH gave readings averaging 2.5×10^{-6}; three blanks averaged 1.3×10^{-6}. Thus, the net iodide concentration was $(2.5 - 1.3) \times 10^{-6} = 1.2 \times 10^{-6}$ NI^-. The concentration

of UDMH was $\frac{1.79 \times 10^{-6}}{60.1} \cdot \frac{1}{0.05} = 5.96 \times 10^{-7}$ M; thus, the ratio of I^- ions to UDMH molecules is $\frac{1.2 \times 10^{-6}}{5.96 \times 10^{-7}} \simeq 2$ I ions per molecue.

4.2.2 The sensitivity of the method can be calculated as follows: 1 ppm (g) = 2.45×10^{-6} g/liter = 4.07×10^{-8} moles/liter.

10 minute sample, 1 lpm into final volume of 0.05 liter (solution) conc = $\frac{10 \times 4.07 \times 10^{-8}}{0.05} = 8.14 \times 10^{-6} \frac{\text{moles UDMH}}{\text{liter}}$, which would yield 1.63×10^{-5} N I^-; therefore, under these sampling conditions (10 min., 1 lpm, 50 ml final volume). conc. (ppm, gas) = $\frac{\text{net conc}}{1.63 \times 10^{-5}} = \frac{C \times \text{net scale reading}}{1.63 \times 10^{-5}}$ = $\frac{1 \times 10^{-5} \times \text{net scale reading}}{1.63 \times 10^{-5}}$, or 0.613 x net scale reading.

The scale is readable from about 0.05 to 10, which would correspond to net leakage concentrations of about 0.03 ppm to 6.1 ppm.

Similar results were obtained with hydrazine and monomethyl hydrazine. However, as with the various colorimetric tests, no hydrazines were detected during canister gas testing.

4.5 HNU Photoionization Analyzer Calibration

The general procedure for calibrating this device was to make a bag mix of a few ppm of the appropriate hydrazine, analyze the bag mix colorimetrically, and use this information to calibrate the instrument.

The results of this approach were (with the instrument at its maximim sensitivity): hydrazine: 4 divisions for 0.1 ppm
monomethyl hydrazine; 5 divisions for 0.2 ppm
1,1 dimethyl hydrazine: 15 divisions for 0.5 ppm

These are not as large a signal as one might desire. However, they demonstrate that the instrument is capable of detecting hydrazines at the TLV level. (The colorimetric and iodometric results indicate that the penetrating gases are not hydrazines; breaks signalled by the photoionization instrument are probably caused by ammonia, amines, and possibly methane and methanol.)

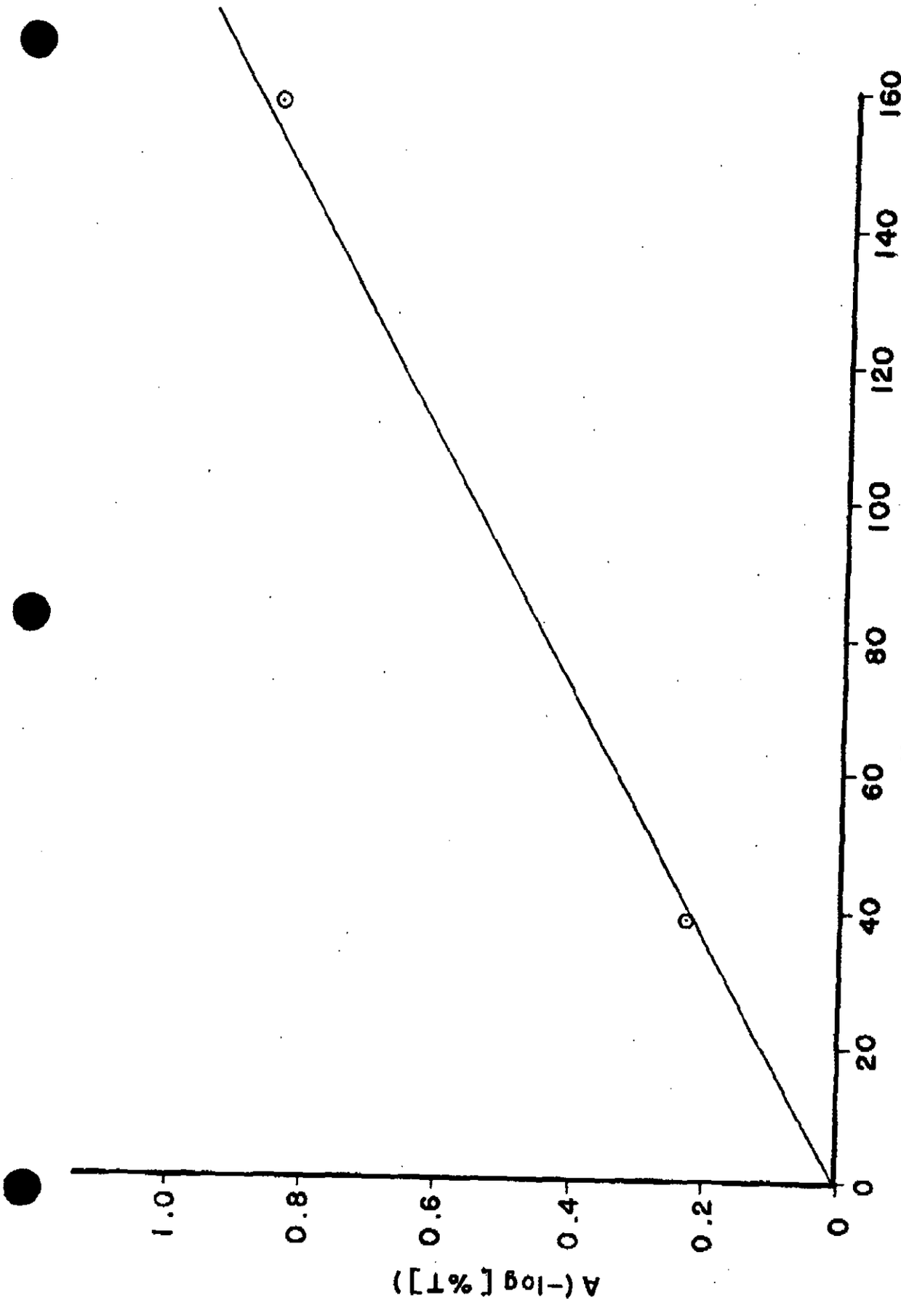

FIGURE 4. TYPICAL COLORIMETRIC CALIBRATION FOR UDMH

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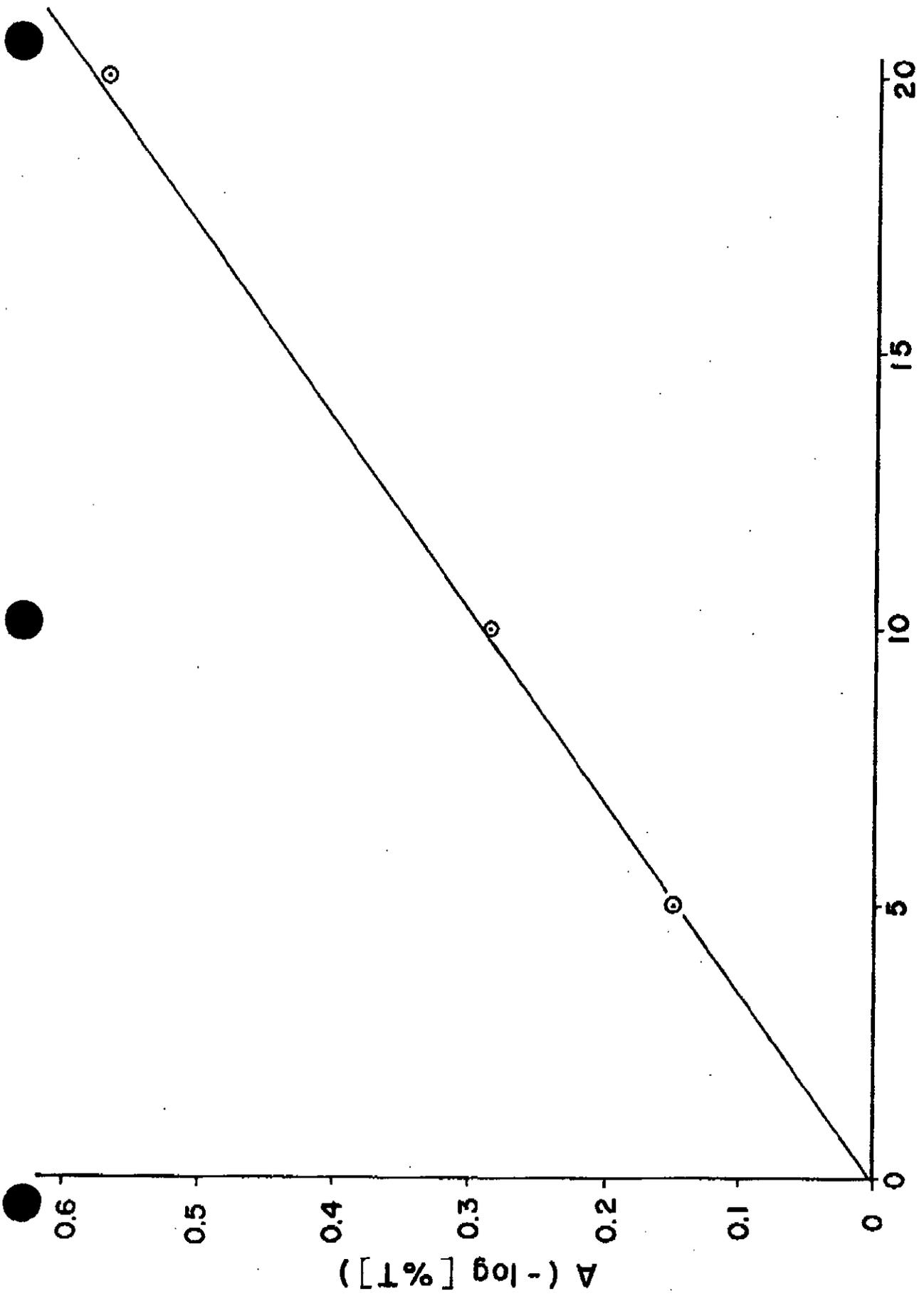

FIGURE 5. TYPICAL COLORIMETRIC CALIBRATION FOR HYDRAZINE

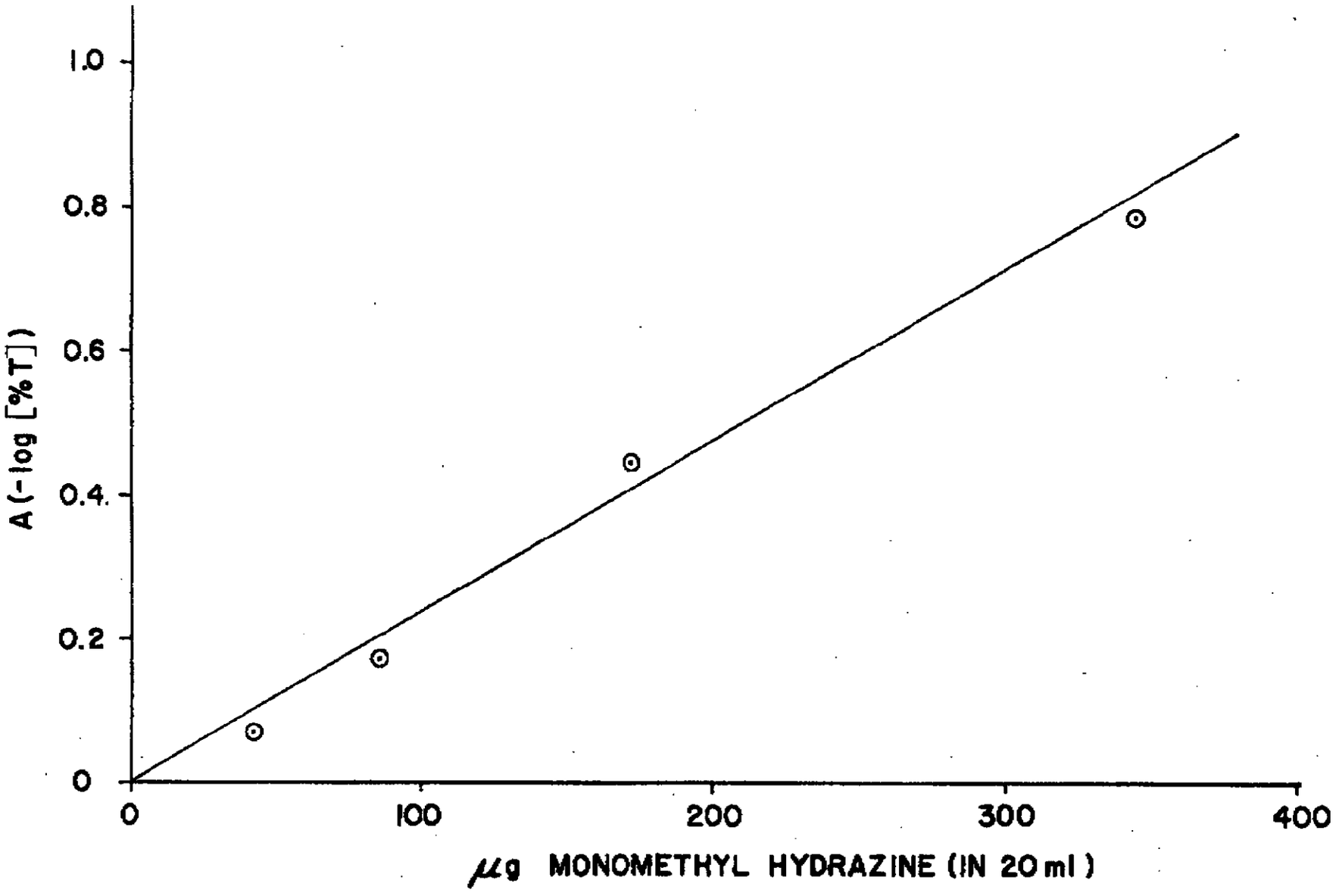

FIGURE 6. TYPICAL COLORIMETRIC CALIBRATION FOR MONOMETHYL HYDRAZINE

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MAY-04 98 00:22 FROM:

TO:8185869295

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PROCEDURE FOR

LABORATORY (PB)

ACTIVITIES

Propulsion Research Area (PRA)
PROPULSION FIELD LABORATORY
ROCKETDYNE

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Revised: October 1960

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INTRODUCTION

The following pages outline procedures to be used for pentaborane (PB) activities in the Propulsion Research Area (PRA). They are to be used in conjunction with well instructed personnel and a suitable description of PB and its problem areas. Temporarily, until a suitable section of PFA/59/3 (Propellant Field Use Manual) is written for PB, the Olin Mathieson Chemical Corporation technical Bulletin LF202, June 1960, will serve for description of PB and its problem areas.

Any comments, corrections, additions, etc., should be submitted to the authors.

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PART I

PROPULSION RESEARCH AREA (PRA)

PROCEDURES

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A. PERSONNEL PROTECTION

1. Respiratory (Figure 1)

a. Test Pit Area

1. Self-contained Scott Air Paks with pressure demand feature for test pit area and control center. (See below.)/or

2. Self contained Scott Air Paks in conjunction with manifold extension of #b below.

b. Control Center - Air conditioning is turned off at the start of PB handling and is kept off until PB hazard is gone.

1. Fresh Air Inlet Duct. This duct will provide positive pressure to control center; wind direction-and-velocity indicator is located near entrance to duct and is monitored in control center.

If wind direction (Fig. 2) is correct, fresh air inlet duct can be used during propellant transfer, pre- and post-firing inspections, decontaminations, etc. For firing activities, see below.

2. Breathing Air Manifold System (Fig. 1)

a. While fresh air inlet duct is operating, personnel will have Scott Air Pak harness on and mask over shoulder, but bottle need not be worn.

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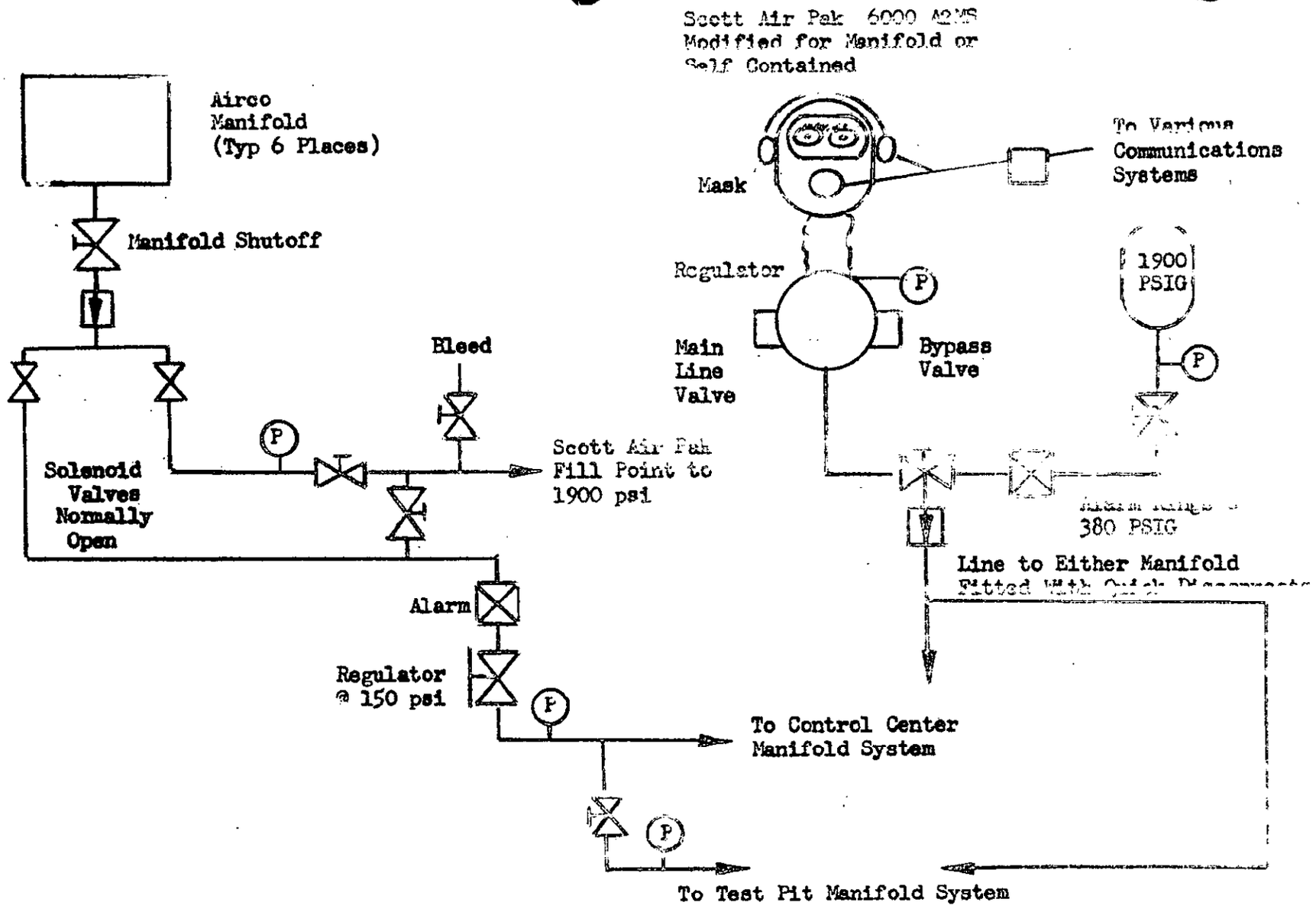

PROPULSION RESEARCH AREA BREATHING AIR SYSTEMS
MANIFOLD AND SCOTT AIR PAK FILL

Figure 1

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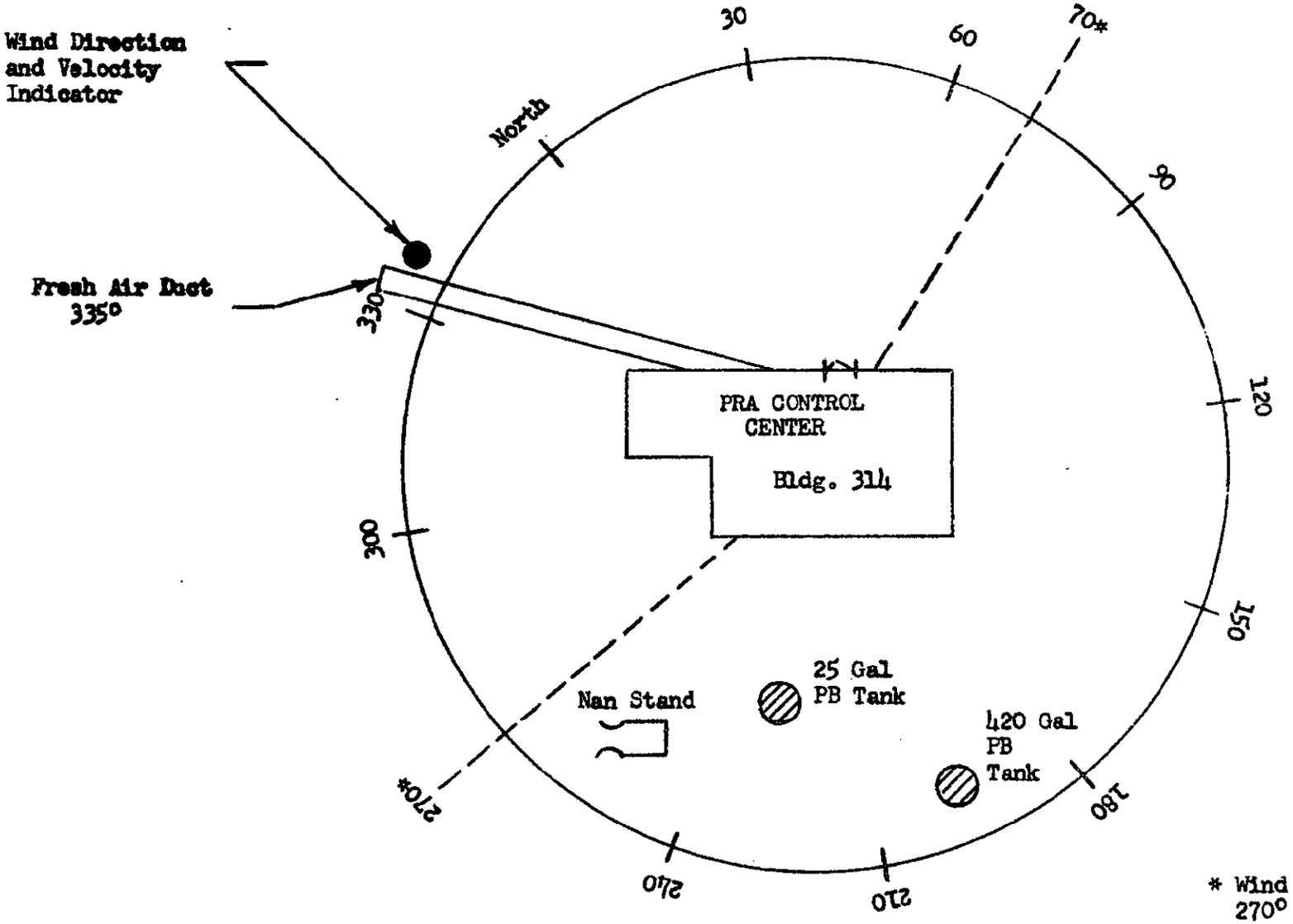

* Wind Blowing From 270° to 70° is Satisfactory for Firing, Transfer Decontamination, etc.

WIND RELATIONSHIPS IN PRA
FIGURE 2

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b. If wind speed or velocity changes adversely at duct entrance, during transfer, pre- and post-firing inspection, decontamination, etc., mask will be put on and air will be supplied by manifold and fresh air inlet duct will be turned off. Duct can be turned on again and masks taken off at discretion of Responsible Project Engineer.

c. During PB tank pressurization and test firings, personnel will be on manifolded system. Fresh air inlet duct will be off.

2. Skin

a. General. At start of PB test activities, all personnel in PRA will change into flame-proof coveralls. All personnel will wear boots (Tingly Neoprene) for personal protection and to minimize taking any contamination out of PRA and home from PFL. A Decon boot bath will be used to prevent contaminating the PRA control center and workshop. Also, see Part III E.

b. Control Center Clothing (See A.2.a)

c. Test Pit Operations. While test pit area is in hazardous condition, all personnel are to wear Gra-lite suits and hood, Neoprene boots, and Gra-lite gloves. A hazardous condition is to be determined by Responsible Project Engineer.

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3. Detection

a. (See Photo No. 1222 8/9/60 S1E) The Olin Mathieson Demon type borane monitor, a semi-automatic, continuous borane detection device of exceptional sensitivity will be used. This detector is sensitive to temperature changes and to other propellants. The Responsible Project Engineer is responsible for seeing that this detector is in proper working order.

B. DECONTAMINATION

1. Normal

a. Test Hardware, Tools, PB Systems (See Part II)

b. Propulsion Research Area

1. Survey entire area during loading and both before and after test firing with Demon borane monitor and attempt to determine levels of contamination.

2. Test Pit Area - PRA

a. After PB test activities are over for day

1. water wash with rainbirds and firex system

2. Decon wash (3% NH_3 solution and detergent) (see Section III-D)

3. water wash

4. survey area with Demon borane monitor

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3. Control Center and Shop

a. After PB test activities are over for day

1. survey with Demon borane monitor

2. blow out with fresh air duct or air conditioner.

c. Personnel (See Section III-E)

d. PB Spills

1. If spilled PB does not ignite, it will be ignited with a flare and allowed to burn. Adjacent areas will be protected with Firex systems.

2. Decontamination of area will proceed as in Part B.1.-b.2

C. TEST OPERATION PROCEDURES, GENERAL PLAN TOC

1. PRA - TOC - PFL Relations

a. Brief description of Test Operations Control Center (TOC)

1. PRA test activity with special propellants such as PB is monitored by the PFL Test Operation Control Center (TOC). The TOC can be reached by the yellow phone in the PRA Control Center, and on Ext. 5600 on the regular phone system. Briefly, the functions of TOC are as follows:

a. Act as a central schedule recording agency for all large engine test activities and all special propellant test activities at PFL, including Components and Research.

b. Provide a central communications service for transmittal of run status information to Industrial Security and other interested departments.

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c. Maintain a display of PFL which reflects the instantaneous status of all test activities.

d. Control visitors' tours of the test areas.

e. Provide meteorological control for testing with special propellants.

f. Determine amount of special propellants to be used in test areas and control test activities on the basis of meteorological conditions.

b. For weekend and evening operations, virtually all of Area I will be closed as well as PRA. TOC will determine such closure in conjunction with PRA engineers.

c. Securing PRA for PB activities other than weekend

1. Check with TOC by 9:30 AM of the test day about wind conditions for the day.

2. Notify TOC 30 minutes prior to the test or propellant transfer operation and get permission to proceed. TOC will advise if a roadblock is required and what areas will be evacuated.

3. Notify PRA by public address with a suitably worded announcement that the test or transfer is 15 minutes away from being accomplished.

4. Notify the following activities at 15 minutes before a test or transfer that a test or transfer (indicate which) is about to be made and to evacuate the area. Receive confirmation.

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TOC . . . . . Yellow Phone

* NAKA . . . . . Ext. 5307

* PEROXIDE . . . . . Ext. 5306

* TUNNEL . . . . . Ext. 5305

* CHEM. ENGR. LAB. . . . . Ext. 5341-5342

* HAPPY VALLEY . . . . . Ext. 5412

* FUEL DUMP . . . . . Ext. 5050

* These activities can be warned and a confirmation received by the overall Research Area paging system (All Call).
Activities not listed here will be notified and given instructions by TOC.

5. Give a suitable worded public address announcement and blow 3 - one-second siren blasts at 3 minutes prior to the test. Raise the red flag and turn on the PRA red lights.
6. At 20 seconds, blow single ten-second siren.
7. Time: ZERO - FIRE.
8. After venting, TOC, in conjunction with project engineer, will determine when specific activities outside of PRA can be resumed.
9. PRA will be cleared, when project engineer determines area is not contaminated, by a series of horn blasts, paging system announcement, and changing visual indicators from red to yellow.
10. Notify TOC and adjacent areas that PRA is clear

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2. PRA - Restricted Areas

PRA restricted areas will be posted:

a. Contaminated Area

While test pit area and test stand is contaminated, as determined by responsible area engineer, all PRA is restricted to authorized "test personnel" and emergency personnel only.

b. After Decontamination

Restricted areas, as posted, will be limited to those people specifically authorized by Group 591-361 Group Scientist or designee. Man stand personnel will wear protective clothing as required by responsible project engineer for test stand operation.

c. Overnight and weekend restricted areas (see Section III-F).

3. Communications

The following communication systems are available for the Man stand PB tests.

a. TOC phone (yellow) - This phone can be spoken into from Scott Air Paks through Voicecaster.

b. Regular telephone (black) same as TOC phone for Scott Air Paks.

c. Roadblock phone (black) same as TOC phone for Scott Air Paks.

d. Local pit phone system

e. Local PRA paging system, same as TOC phone.

f. Overall Research paging system (All Call) same as TOC phone.

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4. Public Address Announcements

It is suggested that the announcer take time to write the announcement and read it carefully over the PA system. Repeat each announcement twice. It is essential that announcements are clear and that all areas are continually kept informed of all test activity if it deviates from that which has previously been announced.

The 15 minute announcement should be repeated twice and state that the test or transfer is 15 minutes away.

Following is a suggested 3 minute announcement:

Test Firing: Your attention please - - - -
There will be a firing (or sequence of firings) on Nan stand in test pit one. Please clear the test pit area. The propellants will be pentaborane and hydrazine.

Repeat! Be Clear ! Keep All Areas Informed!

Then Blow 3-Minute Sirens!

D. EMERGENCIES

1. Working Hours

In case of suspected exposure to toxic boron compounds, call Ext. 5333 for rescue crew and, if available, nurse. Give the following on-the-spot treatment.

a. Eye Contact - flush with water

b. Skin Contact - flush with water. Burned clothing to be removed by both fire department and PRA personnel.

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c. Inhalation - give oxygen and call fire department rescue.

2. After Working Hours

If adverse symptoms such as visual disturbance, muscle weakness, impaired coordination, drowsiness, tremor or profuse sweating appear, give oxygen and call ROCKETDYNE CONTROL CENTER

6633 Canoga Avenue, Canoga Park, California

Diamond 7-5651, Extension 2351

Report Pentaborane Symptoms

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PART II

PRA NAN STAND AND PENTABORANE FLOW SYSTEM PROCEDURES

PHOTOGRAPHS AND DIAGRAMS

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PHOTOGRAPHS

1241 - 8/5/60 S1G

The 420 gallon, 3,000 psi pentaborane (PB) propellant feed tank showing pentaborane shipping cylinders hooked up for PB transfer operations.

1241 - 8/5/60 S1R

The bottom of the 420 gallon tank showing the main tank shut-off valve and associated plumbing.

1241 - 8/5/60 S1B

A typical section of the PB flow system showing Sugar Stand prevalve.

1241 - 8/5/60 S1C

View of the rear of Man Stand blast plate showing 2" pentaborane main valve and associated plumbing including micromotor take off points.

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A. 10K AND 30K PENTABORANE FLOW SYSTEM

Figure 3 illustrates a schematic of the pentaborane flow system designed to accomodate Nan Stand. For the sake of clarity, none of the other propellant feed or ignition systems on Nan Stand are shown since they are all conventionally gas pressurized.

The propellant storage tank incorporates dual burst diaphragms, dual vents, and a nitrogen gas purge for flushing the vent lines subsequent to a test firing. All valves on the pentaborane facility are normally closed, i.e., "fail safe", with the exception of the low pressure burst diaphragm closure. In the event of failure of the vent valves to relieve tank pressure, the tank is further pressurized and relieved through the rupture of the low pressure burst diaphragm. The normally open valve can then be closed to prevent pentaborane vapors from continually issuing from the system.

The ends of the vent lines are prevented from being a hazard source through using a nitrogen flush in the vents and sealing the vent lines at the conclusion of the test day's operations.

Once the shipping cylinders are connected, the filling operation is remotely handled. Photograph 1241-8/5/60-S1Q shows the pentaborane shipping cylinders next to the 420 gallon propellant feed tank. The cylinders are not disconnected after the filling operation but remain "at the ready" to receive liquid from the run tank if it is desired to empty the pentaborane system. Not only can the pentaborane be

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returned to the shipping cylinders, but it also can be transferred to a 600 gallon catch tank. This catch tank normally holds a dilute toluene-pentaborane solution, received during transfer or decontamination operations. Also provided is a steel burn basin which has been placed in the middle of a 35,000 gallon water sump. The burn basin will be used as required to dispose of the toluene-pentaborane solution. In the event of an emergency the total contents of the run tank can be disposed of in this manner.

A liquid return system has been provided to empty the line between the tank shutoff valve and the main valve at the end of the test day. Since the main propellant system consists of 2 and 3 inch pipe, a considerable quantity of pentaborane is removed from an area of potential danger created by other nearby stands firing. This operation reduces the potential spill hazards involved in the event the main propellant line is damaged by an external malfunction.

Toluene is used as the primary diluent and decontaminant. A gas pressurized tank has been installed and is capable of delivering toluene to any section of the propellant system. Not only is toluene used in the above fashion but it can be used as an inert lead during injector test operations. Photograph 12h1-8/5/60-S1C is a photograph of the main valve system showing the hydrazine and pentaborane main valves and the toluene, helium, nitrogen, and water flushes for the main valve complex.

The following procedures are actually used for test operations by well trained personnel. Because of the very dynamic nature of the PB program, they may not always be up to date in this manual, but generally, they will suffice to insure personnel security.

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B. PENTABORANE FILLING PROCEDURE FOR 420 GALLON RUN TANK

See Figure 3.

1. Unplug vent lines and open vent closure.
2. Check PB tank pressure, if more than 20 psig, open emergency vent and vent tank.
3. Place 15 psig of helium on helium flush hand loader.
4. Open cylinder flush.
5. Connect helium pressurizing line to points G1 and G2.
6. Open cylinder by-pass.
7. Connect helium line to points L1 and L2.
8. Open catch tank valve.
9. Open catch tank vent.
10. Open #2 disposal. Adjust helium to 25 psig.
11. Open fill #1.
12. Close fill #1 and open fill #2.
13. Close fill #2.
14. Close catch tank vent.
15. Close cylinder by-pass and cylinder flush.
16. Close disposal #2.
17. Adjust helium pressure to 75 psig.
18. Open G1 and check pressure in bottle.
19. Vent bottle to 75 psig by cylinder vent if necessary.
20. Open L-1.
21. Open fill #1.

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PENTABORANE FILLING PROCEDURE FOR 420 GALLON RUN TANK (Cont'd)

22. Open main-fill.

23. Open cylinder flush.

24. Empty bottle.

25. Close cylinder flush.

26. Close main fill.

27. Close fill #1.

28. Open G2 and check pressure in bottle #2.

29. Vent bottle to 75 psig by cylinder. Vent if necessary.

30. Open L2.

31. Open fill #2.

32. Open main-fill.

33. Open cylinder flush.

34. Close main fill.

35. Close fill #2.

36. Vent bottles to 10 psig.

37. Reduce helium pressure to 25 psig.

38. Open and close disposal #2.

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C. PENTABORANE LIQUID RETURN TO CYLINDERS FROM 420 GALLON RUN TANK

See Figure 3.

1. Vent pentaborane tank to 10 psig max.
2. Check that G1, G2, and L1 and L2 are open.
3. Open main fill.
4. Open fill #1.
5. Fill bottle to desired level.
6. Close fill #1.
7. Open fill #2.

   Fill bottle to desired level.
8. Close fill #2.
9. Close main fill.
10. Close L1, L2, G1, and G2.

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D. PENTABORANE CYLINDER DISCONNECTION FROM 420 GALLON RUN TANK FILL SYSTEM

See Figure 3.

1. Set helium to 25 psig.
2. Check that sufficient toluene in catch tank.
3. Open catch tank valve and catch tank vent.
4. Open disposal #2.
5. Open fill #1.
6. Open TOL #1.
7. Flow toluene for 15 seconds.
8. Close TOL #1.
9. Close fill #1.
10. Open fill #2.
11. Open TOL #2.
12. Flow for 15 seconds.
13. Close TOL #2.
14. Open cylinder flush and cylinder bypass.
15. Purge for 15 seconds.
16. Close fill #2 and open fill #1.
17. Purge for 15 seconds.
18. Close fill #1 and cylinder flush and cylinder bypass.
19. Repeat steps 5 through 18.
20. Close disposal #2 and catch tank valve and catch tank vent.
21. Reduce helium pressure to 15 psig.
22. Open cylinder bypass and cylinder flush.
23. Disconnect L1 and L2; cap and plug.
24. Close cylinder bypass.
25. Disconnect G1 and G2; cap and plug.
26. Close cylinder flush.

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E. TRANSFER OF PENTABORANE TO CATCH TANK FROM 420 GALLON RUN TANK

See Figure 3.

1. Ascertain that PB tank pressure is vented to 50 psig or below.
2. Open catch tank fill.
3. Open emergency dump.
4. After emptying tank section, open tank shut-off and dump.
5. Open Nan prevalve, close dump and open #3 disposal.
6. Close #3 disposal and open #4 disposal, then close #4 disposal.
7. Empty toluene tank into catch tank for diluent effect percentage of Pentaborane of at least no greater than 40%.
8. Close L1 and L2.
9. Open TOL #1.
10. Open TOL #2.
11. Open fill #1.
12. Open fill #2.
13. Open disposal #2.
14. Close valves in Steps 9 through 13.
15. Refill toluene tank if necessary and repeat Steps 9 through 14.
16. Vent catch tank if necessary during disposal.

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F. DISPOSAL OF PENTABORANE FROM 420 GALLON RUN TANK INTO SUMP AND BURNING

See Figure 3.

1. In the event it is desired to dispose of the pentaborane directly into the sump and burn it, the following procedure should be followed:

   a. Transfer 30 gals of toluene into the sump burn off container by following steps b through f.

   b. Ascertain that L1 and L2 on PB cylinders are closed.

   c. Open TOL #1 and TOL #2.

   d. Open fill #1 and fill #2.

   e. Open disposal #2.

   f. Open pond valve to water sump.

   g. When approximately 30 gals are delivered to the sump, about 1/2 to 1 inch layer of toluene on the water surface, close valves opened in steps b through f.

   h. Remotely ignite surface of toluene floating on water by actuating igniter switch on consol, after placing ignitor in the sump.

   i. After flame is established, commence disposing of PB in small quantities as follows: (keep PB tank pressurized to between 10 and 20 psig).

   j. Cycle emergency dump.

   k. After completing the emptying of the tank section, close emergency dump, open tank shutoff and main dump.

   l. Open Nan prevalve, close main dump and open #3 disposal.

   m. Close #3 disposal and open #4 disposal.

   n. Close #4 disposal.

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G. COMPLETE SYSTEM DECONTAMINATION IF REQUIRED AFTER DISPOSING OF PENTABORANE

The system should be completely filled with toluene and held for a sufficient period of time (3 to 8 hours) to insure that all PB is dissolved in toluene and disposed of by burning in the same manner as above.

The system should then be filled with the 3% NH_3 solution and held for two days. Since considerable hydrogen evolution will occur allowance must be made for the gas to escape.

The system should then be filled with an alcohol water solution and held for two more days.

The system can then be washed with water, dried, and monitored with PB detector.

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H. DECONTAMINATION OF HARDWARE, HAND TOOLS, AND EQUIPMENT

1. Prior to test operations, containers of a decontamination solution are placed in PB contaminated drum storage area. The solution for brevity will be referred to as Decon.

2. After transfer or test firings are completed and tools or hardware are to be contaminated, the following procedures should be followed:

   a. Prime the PB injector dome with toluene before working on the motor.

   b. Purge PB dome at low purge pressures.

   c. Remove instrumentation and plug the PB injection pressure line.

   d. Disconnect CTF lines and plug.

   e. Disconnect hydrazine lines and plug.

   f. Disconnect PB line and plug.

   g. Remove hardware and place in Decon.

   h. All tools used in the test operation are to be washed with water and then placed in Decon; then rinse tools with water and place in ethyl alcohol.

   i. The test area is ready for hosing down with Decon, See Part I-B.

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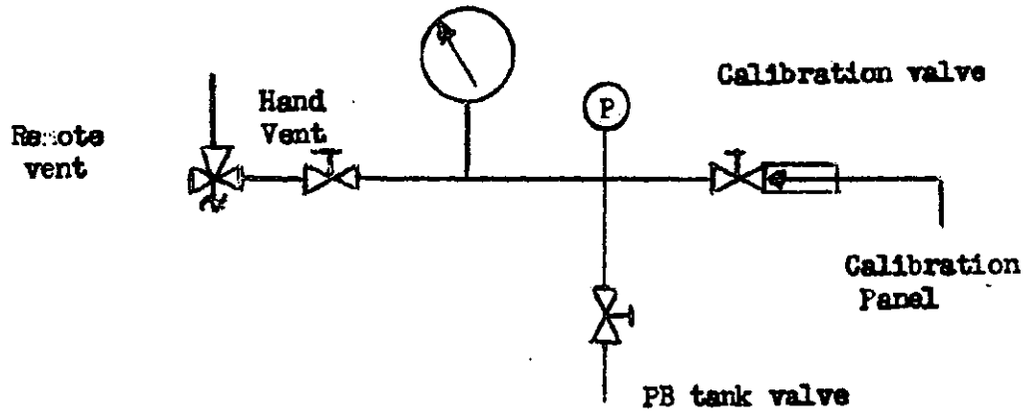
I. CALIBRATION PROCEDURE FOR PENTABORANE TANK



1. Close PB tank valve.
2. Open hand vent.
3. Place calibration pressure on panel at higher value then in PB tank.
4. Open calibration hand valve.
5. Open remote vent and purge for 3 minutes.
6. Reduce calibration pressure to ZERO.
7. Commence calibration by closing remote vent and applying pressure from panel.
8. After calibration pressure reached, open remote vent before reducing pressure on calibration panel.
9. After calibration completed, close remote vent, calibration valve and hand vent.
10. Open PB tank valve.

J. PENTABORANE SYSTEM INSPECTION

All valves, fittings, flanges, etc., on the 10K and 30K pentaborane flow system will be inspected for pentaborane leakage, both visually and with the Demon borane monitor weekly. The responsible project engineer is responsible for setting up a weekly inspection schedule and for seeing that this system is free from leakage.

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PART III

OTHER PROCEDURES

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A. Equipment Laboratory*

1. Introduction

All items, such as valves, test hardware, etc., which have been used in Pentaborane must be decontaminated at the test site, packaged in open packages and properly tagged according to REPM IV-13 prior to shipment to E.L. for service.

REPM IV-13 specifies the general procedures that the test site and receiving organizations, such as E.L., will follow when receiving decontaminated items.

2. Special Test Site Decontamination Procedure for Items Used in Pentaborane: To be Performed by Test Site Personnel.

The following decontamination procedure will be used for decontaminating items used in Pentaborane:

a. Disassemble item, if there are several component parts, in 3% (weight) ammonium hydroxide plus 3% (weight) detergent solution. Immerse one piece items. Discard all non-metal parts in suitable contaminated containers for subsequent destruction.

b. Rinse with water.

c. Immerse in 92.5% ethyl alcohol.

d. Rinse with water.

e. GN_2 dry.

f. Examine with Demon Pentaborane detector.

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g. Packaged in open container.

h. Tag according to REPM IV-13.

i. Ship to E.L. E.L. will take suitable precautions according to REPM IV-13 and the PFL Safety Department and subsequently service the items. Items will be returned to test site according to REPM IV-13.

---

* Reference: IOL dated 18 May 1960 to Those Concerned, From R. K. Hanks, Jr. and M. C. Blum, "Servicing, By the Equipment Laboratory (E.L.) of Items Used in Pentaborane".

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Date _____

PENTABORANE CHECKOUT LIST

I - AREA CHECKOUT

A.- SUMP

1. Gates _____
2. Drain _____

B.-FIREX SYSTEM (Morning of Test)

1. Tank Farm _____
2. Pit #1 _____
3. Catch Tank _____
4. Floor Flush _____
5. Flame Bucket _____
6. Safety Showers _____

C.-DECON SYSTEM

1. Supply Tank (Gal) _____
2. Pump _____
3. Foot Bath _____
4. Hardware Bath _____
5. Tool Bath _____

D.-PRESSURIZING GAS SUPPLY

1. Helium Pressure _____
2. Open PRA Valve from CTL-I _____
3. Open Pit #1 & #2 Hand Valves _____
4. GN_2 Pressure _____
5. CTL-III GN_2 Bottles _____

E.-SAFETY

1. Breathing Bottle Bank
   (1)___ (2)___ (3)___ (4)___ (5)___
2. Scott Paks _____
3. Gra-Lite Clothing _____
4. Cotton Coveralls _____

F.-COMMUNICATIONS

1. Head Phones _____
2. CKT #1 _____
3. T.V. Camera _____

G.-MISCELLANEOUS

1. Boron Detector _____
2. Air Duct & Block House Vent _____
3. TCC _____
4. Fire Dept. Equipment _____

II - STAND CHECKOUT

A.-TANK FARM	Hydrazine	NTO or CTF	Toluene	Water
1. Skinner Pressures	____	____	____	____
2. Valve Checkout	____	____	____	____
3. Micro Switch Lights	____	____	____	____
4. Pressurize to 50 or 100# Psig	____	____	____	____
5. Statham	____	____	____	____
6. Pressure Gauge	____	____	____	____

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TEST PROCEDURE

A. Pentaborane system valve checkout

1. Begin assembly of PB main line
2. Uncap PB vents
3. Purge vent lines
4. Open PB cylinder valves
5. Open dump tank fill (catch tank fill valve)
6. Check valve activation and micro switch indicators
7. Vent PB tank for zero
8. Open PB shut-off and Pre-valve
9. After 3 minutes pressurize PB tank to 200 psi
10. Check for PB leaks
11. Vent PB tank

B. Firing procedure

1. Vent all propellant tanks
2. Check that all purges are off
3. Take preliminary zeros
4. Set PB injector purge loader to 300 psi
5. Turn on PB transducer purge
6. Turn on CTF purge
7. Operate PB & HZ valve purges for 5 seconds simultaneously
8. Open PB injector purge
9. Open gas sample purge
10. Open HZ main - 1 second bursts until primed
11. Turn on HZ injector purge for 10 seconds
12. Turn off PB injector purge when clear

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13. Pressurize NTO tank.

14. Pressurize HZ tank.

15. Adjust PB injector purge to 800 psig.

16. Place breathing air equipment on.

17. Pressurize PB tank.

18. Cut NTO purge.

19. Cut gas sample purge.

20. Cut PB transducer purge.

21. Take photocon zeros.

22. Open gas sampling purge.

23. Cycle PB valve purge.

24. Cycle PB transducer purge.

25. Open water main.

26. Start count-down.

    (1) Open PB injector purge.

    (2) Open HZ injector purge.

    (3) F I R E

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POST FIRING PROCEDURE

1. Flame bucket and floor flush
2. Purge NTO line
3. Close water main
4. Close gas sample purge
5. Trip injection purge relay
6. Close HZ injection purge
7. Open PB transducer purge
8. Open HZ valve purge
9. Close PB injection purge
10. Open toluene flush
11. Cycle PB valve purge
12. Cut all purges for zeros
13. Chart drive
14. If another test is not programmed immediately, run down all loaders and close pressurizing valves.
15. Vent NTO tank
16. Vent HZ tank
17. Vent water tank
18. Vent PB tank
19. Commence liquid return when test period completed.

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D. DECONTAMINATION SOLUTION SYSTEM IN PRA

A 9000 gallon decontamination ("Decon") solution (3% ammonia plus a.1% detergent - Lever Bros. DW 300-in water) storage and use system is now available in PRA. The solution is pumped from the 9000 gallon storage tank to the PRA test pit area, Nan Stand, the pentaborane propellant feed system area, and the personnel decontamination facility. In the test pit area, two rainbirds are mounted and piped to both the "decon" system and to a fresh water system so the entire test pit and tank farm areas can be decontaminated and rinsed remotely from the PRA control center. Also, Nan Stand has a remote "decon" system similar to the present firex system so the stand can be decontaminated remotely from the control center. The Nan Stand firex system will be used to rinse away the "decon" solution. Also, hose bibs are located at strategic places throughout the test pit area to facilitate decontaminating of tools, hardware, transducers, etc.

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E. PERSONNEL DECONTAMINATION IN PRA

A shower and change facility is available in PRA for personnel decontamination at the daily cessation of pentaborane test activities. The facility has four rooms, a "not contaminated" change room, a shower room, a "contaminated" change room, and a toilet. The contaminated room is only considered contaminated immediately after test activities and will be decontaminated as soon as is possible after each test activity.

The following procedures will be followed by all personnel engaged in pentaborane test activities; that is, by all personnel who will actually be in the control center during the pentaborane testing.

1. At the start of any pentaborane test activity, personnel will enter the "not contaminated" change room and change into flame-proof coveralls and neoprene boots.
2. They will then proceed to the "contaminated room" and get in the Gralite suits, hood, and gloves and proceed to their test activities.
3. After the test activities are over for the day, personnel will wash their Gralites in Decon and water at the entry to the "contaminated" change room.
4. Personnel will then hang the Gralites to dry on the racks provided in the "contaminated" change room.
5. Neoprene boots will also be washed, and a washer and dryer are available to wash the flame-proof coveralls.

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6. Contaminated coveralls which will be soaked overnight in "Decon" solution can be washed the next day.

7. The "contaminated" change room will be washed down before leaving for the day.

8. Personnel will then proceed to the shower room and wash with green soap.

9. After showering, personnel can put on the "street" clothes.

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TO: Those Concerned

DEPT.

FROM: M. C. Blum

DEPT. 591-361 PHONE 5667

AVOID VERBAL ORDERS

INTER-OFFICE CORRESPONDENCE

SUBJECT: Securing of the Propulsion Research Area (PRA) Test Pit Area Outside of the Basic PRA Work Week

DATE: 28 October 1960

The basic PRA work week is from 7:30 A.M. to 4:00 P.M. Monday through Friday, holidays excepted.

In order to protect any personnel who might wish to work in the PRA test pit area from the potential hazards of the Pentaborane Storage and Use system, the following procedures are established for use outside of the basic PRA work week.

1. The PRA test pit area will be chained and posted at all entry points. The PRA Group 591-361 leadman or his designee will be responsible to see that this is done daily and on weekends.

2. Anyone desiring to work in the PRA test pit area must notify Industrial Security, X5485, upon entering and leaving the test pit area. He must leave the name of the person who is responsible for the work to be conducted and the total number of personnel involved.

M. C. Blum
Senior Research Engineer
Liquid Propulsion
Research

Approved:

9/59/11

G. S. Gill
Group Scientist
Liquid Propulsion
Research

MCB:rs

cc: Research Supervision
Maintenance
Industrial Engineers
Industrial Security
E. L.
Fire Dept.

W. Colwell D/591-361
R. Gordon D/551
E. Higgins D/551
H. Weiss D/596-162

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10-27-60

NANETTE PROCEDURES

I. Area Checkout

A. See attached sheet

II. Pre-run Procedures

1. N_2H_4 and CTF Priming Operations

a. Open tank shut-off

b. Open hand valve

c. Open pre-valve (remote)

d. Open hand bleed valve and close

e. Close pre-valve (remote)

2. Prime CTF line

a. Hook up CTF bleed line to #4 Main valve

b. Open Nan tank shut-off and pre-valve

c. Open pre-valve (remote)

d. Pressurize CTF tank to 50 psi

e. Open main valve #4 until system is primed

f. Close pre-valve (remote)

3. Set gas and liquid purge pressures

a. N_2 for CTF - 100 psig

b. He for PB - set after run to 25 psig

c. He for P_c - 300 psig

d. Pressurize water tank - 100 psig

e. Pressurize toluene tank - 100 psig

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B. Pentaborane Operations - GRA-LITE

1. Begin assembly of PB main propellant lines

Same procedure as Nan stand

2. Uncap PB vents
3. Purge vent lines
4. Open PB cylinder valves
5. Make complete stand checkout on PB system

6. Open hand valve #1
7. Open PB remote pre-valve and then bring personnel inside
8. Vent PB tank for zero
9. Open Nan PB shutoff and pre-valve
10. After 3 minutes, pressurize to 200 psig
11. Check for leaks
12. Vent PB tank to zero pressure
13. Open catch tank vent, catch tank fill, and Nanette PB remote dump, in that order to relieve pressure in PB system
14. Close valves opened under #13.
15. Close PB remote pre-valve and then send personnel out to complete priming
16. Open sight gage gas escape valve.
17. Open PB remote pre-valve and observe until liquid flows into sight gage
18. If liquid does not flow into sight gage, close PB remote pre-valve and do the following:
    a. Open the catch tank vent, catch tank fill and Nanette PB remote dump
    b. Open the PB remote pre-valve until liquid flows into sight gage, then close PB remote pre-valve
    c. Close the catch tank vent, catch tank fill and PB remote dump
    d. Close the sight gage gas escape valve and bring personnel inside.

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III. Test Procedures

A. Turn on P_c and CTF N_2 purges

B. Open purge check-out switch (H_2O and Toluene)

C. Open toluene (PB) flush until liquid is visible

D. Open water (Hz) flush until liquid is visible

E. Close purge check-out switch (H_2O and toluene)

F. Turn off P_c and CTF N_2 purge

G. Turn on deck and overhead firex until toluene is clear

H. Take pre-zeros

I. Open all pre-valves

J. Pressurize tanks

K. Turn on deck and overhead firex

L. Turn on P_c purge

M. Select engine and turn on CTF on Count of #1

N. Start sequence when CTF is visible

IV. Post-run Decontamination Procedures

1. Commence liquid return, capping of vents and closing of cylinder valves

2. Ascertain that helium pressure from valve purge is set at 25 psig

3. Cap up PB main lines after thoroughly flushing with toluene and then thoroughly purging with helium

4. Ascertain that PB remote pre-valve is closed, and open hand valve #2

5. Open catch tank fill and Nanette PB remote dump

6. Open helium flush

7. Open PB main valves one at a time, commencing with motor #5 leaving them all on.

8. Close PB remote dump

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9. Vent catch tank. Ascertain that workshop is closed prior to venting. Close catch vent valve

10. Close hand valve #1

11. Open sight gage valve

12. Open PB remote dump

13. When liquid is purged out of sight gage, close helium flush, then PB main valves

14. Vent catch tank

15. Close all open remote valves

16. Close all hand valve on Nanette

17. Remove all hardware from test stand and immerse in decon

18. Actuate firex and tank farm washes and floor flushes for 1 to 2 minutes.

19. Actuate decon system for 30 seconds

20. Repeat step #18

21. Examine test area with Olin Mathieson Demon Boron Detector.

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APPENDIX A

Glossary of Terms Related to Propellants

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Ambient

Surrounding - encircling. Thus, ambient temperature or pressure is the prevailing temperature or pressure surrounding the material or object in question.

Anhydrous

Free of water.

Atmosphere

A unit of pressure equal to 14.7 psi at sea level.

Auto-Ignition

The lowest temperature at which a substance in contact with air (or other oxidizer, if specified) will ignite spontaneously and continue to support combustion.

Boiling Point

The temperature at which the vapor pressure of a liquid becomes equal to the pressure of the ambient atmosphere.

Catalyst or Catalytic Agent

Any substance which, by virtue of its presence, affects the rate of a chemical reaction, and which may be recovered practically unchanged at the end of the reaction.

Compatible

Having no undesirable effect with or upon another material under specified conditions of use.

Corrosive

A material which acts upon another material in such a way as to destroy or damage it permanently. Example: Acid destruction of the interior of a pipe or tubing installation.

Critical Pressure

The existing pressure at the critical temperature.

Critical Temperature

The highest temperature at which a gas can be liquified without regard to the pressure applied.

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Cryogenic

A liquid whose boiling point is at or below that of liquid oxygen.

Ductile

Synonym - pliant of flexible. In rocket usage, we are concerned with a material's ability to remain pliant or flexible at cryogenic temperatures.

Flammable

Combustible. A material which can be ignited.

Flammable (or explosive) Limits, Upper and Lower

Limits established by the richest and leanest mixtures of flammable gas and air that will support flame propagation upon ignition. They are expressed in terms of percentages of gas or vapor in air by volume (e.g., the explosive limits of gasoline are 6% to 1%, and mixtures beyond these limits are too rich or too lean, respectively, to support flame propagation).

Flash Point

The minimum temperature at which the surface of a liquid may be momentarily ignited by an open flame.

Freezing Point

The temperature at which a material changes from a liquid state to a solid state. The freezing point is slightly dependent upon pressure.

Fuel

Any flammable chemical which can burn with an oxidizer.

Hygroscopic

Capable of absorbing moisture from the air.

Hypergolic

A term applied to described self=ignition of a fuel and oxidizer upon contact with each other.

Impervious

Pertaining to clothing which is impenetrable by a chemical.

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Inert

Incapable of producing an effect. In rocket usage, a material which will not burn or support combustion.

Inhibit

To check or retard a chemical action.

Liquid Propellant

A chemical in liquid form used as a fuel, oxidizer, or monopropellant to provide the combustion necessary for the production of thrust by a rocket engine.

Liquid to Gas Ratio

A comparison of the volume of the liquid state of a material at its boiling point to the volume of its gaseous state at standard temperature and pressure (59°F and 14.7 psia).

Example: 1 cubic foot of liquid oxygen, at its boiling point, will evaporate into 862 cubic feet of gaseous oxygen at 59°F and one atmosphere. Therefore, the liquid to gas ratio is 1:862.

Maximum Allowable Concentration

The maximum amount of a toxic gas or vapor which the body can stand for an eight-hour (8-hr.) period in one day, for an indefinite number of days, without causing any injury to health. It is expressed in parts per million (ppm), by volume, of the gas or vapor in air. The majority of rocket propellants are toxic by nature.

Monopropellant

A single material, usually utilized with a catalyst to cause it to react for purposes of powering a rocket engine or some component thereof.

Oxidizers (or Oxidizing Agents)

A chemical that will actively support combustion or oxidation of a fuel.

Padding (or Blanketing)

Filling the void, or ullage, of a closed container with an inert gas (usually nitrogen) to prevent oxidation of the chemical contained therein, and to avoid the formation of flammable or explosive mixtures by excluding air from the container.

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Passivation

The treatment of metals to render them inert to the action of a particular chemical or mixture by the formation of an impervious film on the contact surface.

Psia

Pounds per square inch absolute (14.7 psia = 1 atmosphere at sea level; 0 psia = a complete absence of pressure, or a vacuum).

Pyrophoric

Any fuel or other material which will ignite spontaneously upon contact with air.

Pyrotechnic

A mixture of an oxidizing agent and solid fuel designed to produce light or heat, or to perform some other non-propulsive function. Usually used as igniters.

Psig

Pounds per square inch gauge (0 psig = 1 atmosphere at sea level).

Solid Propellant

A solid mixture consisting of a fuel and oxidizer cured in the form of a block or "grain" which fits into the combustion chamber of the rocket for the production of thrust.

Stability

State of balance; a condition in which opposing forces exactly balance or equal each other. In rocket usage, thermal and shock stability are important. Thermal stability refers to a material's ability to remain stable when a change of temperature occurs, and shock stability refers to a material's ability to remain stable when subjected to shock.

Storable

Refers to liquid propellants which may be stored at or near ambient conditions over a period of time without any chemical or physical change.

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Threshold Limit Value (TLV)

Concentrations of airborne contaminants to which most workers can be exposed during working hours (that is, 8 hours a day, 5 days a week) for indefinite periods without adversely affecting their health.

Toxic

Poisonous, or causing poisoning.

Ullage

Unfilled space in a container.

Vapor Density

The relative density of vapors as compared with the density of air, taken as 1. Example: Acetone vapor density is 2.00; air = 1.00. Acetone vapors are twice as heavy as air.

Vapor Pressure

The pressure exerted by the evaporation of a liquid at any given temperature.

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APPENDIX B

Compilation of Facts

Concerning

Propellant Properties

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CRYOGENICS

	LOX	LN_2	LHe
Boiling Point °F	-297	-320	-452
Freezing Point °F	-361.8	-345.9	-455.8
Vapor Pressure psia	480 @ -200°F	-	-
Vapor Density	1.1	.966	.13
Appearance: Liquid	Pale Blue	Colorless	Colorless
Vapor	Invisible	Invisible	Invisible
Odor	None	None	None
Liq. to Gas Ratio	1:862	1:695	1:754
Vapor Hazard	Asphyxiation below 19.5% Fire Hazard above 24%	Suffocation 1:1 ratio	Suffocation 1:1 ratio

	FLUORINE	FLOX	HYDROGEN
Boiling Point °F	-306	-301	-423
Freezing Point °F	-363.3	-	-434.5
Vapor Pressure psia	794 @ -200°F	574 @ -200°F	147.3 @ -402°F
Vapor Density	1.3	1.2	.069
Appearance: Liquid	Yellow	Greenish	Colorless
Vapor	Brownish	Green-Brown	Invisible
Odor	Pungent	Pungent	None
Liq. to Gas Ratio	1:958	1:890	1:851
Vapor Hazard	Toxic MAC 0.1 ppm	Toxic MAC 0.1 ppm	Suffocation 1:1 ratio
Explosion Limits	Fire Hazard	-	4% to 75%
Ignition Temp.	-	-	1075°F

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STORABLE OXIDIZERS

	MTO	H_2O_2	IRFNA	CTF
Boiling Point °F	70.1	286	197	53
Freezing Point °F	11.84	11	-55	-105
Vapor Press. psia	30.7 @ 100°F	.17 @ 104°F	2.6 @ 160°F	26.6 @ 80°F
Vapor Density	3.2	1.1	3.2	3.2
Appearance: Liq.	Brown	Colorless	Org to Red	Greenish
Vap.	Red to Tan	Invisible	Red to Tan	Grn-Brn
Odor	Pungent	None	Pungent	Pungent
Vapor Hazard	Toxic MAC 2.5 ppm	Toxic MAC 1 ppm	Toxic MAC 5 ppm	Toxic MAC 0.1 ppm

STORABLE FUELS

	HYDRAZINE	MMH	UDMH
Boiling Point °F	236	189.5	146
Freezing Point °F	35	-62.5	-71
Vapor Pressure psia	.31 @ 80°F	1.0 @ 80°F	3.1 @ 80°F
Vapor Density	1.1	1.59	2.1
Appearance: Liquid	Colorless	Colorless	Colorless
Vapor	Invisible	Invisible	Invisible
Odor	Ammonia	Ammonia	Ammonia
Flash Point °F	100 - 126	61 - 63	3
Explosion Limits % by volume at one atmosphere	4.7 - 100 @ 212°F	2.5 - 98 @ NTS	2.3 - 80 @ 77°F
Vapor Hazard	Toxic MAC 1.0 ppm	Toxic MAC 0.2 ppm	Toxic MAC 0.5 ppm

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STORABLE FUELS

	HYDYNE	RP-1	ETHYL ALCOHOL
Boiling Point °F	148	350 - 525	173
Freezing Point °F	-120	-40	-174
Vapor Pressure psia	3.5 @ 80°F		2.6 @ 104°F
Vapor Density	HTA	HTA	1.59
Appearance: Liquid	Colorless	Colorless	Colorless
Vapor	Invisible	Invisible	Invisible
Odor	Ammonia	Kerosene	Alcohol
Flash Point °F	46	110	55
Explosion Limits % by volume at one atmosphere	3 - 45 NTS	1.6 - 6 NTS	3.3 - 19 NTS
Vapor Hazard	Toxic MAC 1.0 ppm	Toxic MAC 500 ppm	Toxic MAC 200 ppm

PYROPHORIC FUELS

	PENTABORANE	TEA	TEB	TEAB
Boiling Point °F	140.1	381.2	171	202.5
Freezing Point °F	-52	-94.5	-166.5	-155.7
Vapor Press. psia	4.0 @ 77°F	.07 @ 181.4°F	.81 @ 68°F	N.D.
Vapor Density	.7 @ 70°F	Flame in air	Flame in air	Flame in air
Appearance: Liq.	Colorless	Colorless	Colorless	Colorless
Vap.	Invisible	Invisible	Invisible	Invisible
Odor	Pungent	Combustion by-products	Combustion by-products	Combustion by-products
Flash Point °F	Pyrophoric	Pyrophoric	Pyrophoric	Pyrophoric
Explosion Limits % by volume at one atmosphere	Flame in air	Flame in air	Flame in air	Flame in air
Vapor Hazard	Toxic MAC .005 ppm	Combustion by-products	Combustion by-products	Combustion by-products

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SOLVENTS

	ACETONE	TRICHLOROETHYLENE
Boiling Point °F	133.7	186
Freezing Point °F	-139	-124.2
Vapor Pressure psia	7.0 @ 104°F	1.9 @ 89.6°F
Vapor Density	2.0	4.53
Appearance: Liquid Vapor	Colorless Invisible	Colorless Invisible
Odor	Mint-like	Chloroform-like
Flash Point °F	0	N.D.
Explosion Limits % by volume at one atmosphere	2.6 - 12.8 NTS	12.5 @ 86°F to 90.0 @ 180°F
Vapor Hazard	Toxic MAC 500 ppm	Toxic MAC 100 ppm

	FREON-MF	FREON-TF	FREON-BF
Boiling Point °F	74.8	117.6	199
Freezing Point °F	-168	-31	+104
Vapor Pressure psia	17 @ 80°F	7 @ 80°F	0.5 @ 80°F
Vapor Density	Heavier than air	Heavier than air	Heavier than air
Appearance: Liquid Vapor	Colorless Invisible	Colorless Invisible	Colorless Invisible
Odor	Irritating	Irritating	Irritating
Flash Point °F	Non-flammable	Non-flammable	Non-flammable
Explosion Limits % by volume at one atmosphere	Non-explosive	Non-explosive	Non-explosive
Vapor Hazard	Toxic MAC 1000 ppm	Toxic MAC 1000 ppm	Toxic MAC 500 ppm

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APPENDIX C

Compilation of Facts

Concerning

Compatible Materials

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CRYOGENICS

MATERIAL	METALS	NON-METALS	LUBRICANTS
Liquid Oxygen	Stainless Steel 18-8 Copper Bronze Brass Aluminum Monel	Teflon Kel-F Asbestos Certain Silicon Rubbers	*
Liquid Nitrogen Liquid Helium	Some Chrome-Nickel Steels (Austenitic-9% Nickel) Stainless Steel 18-8 Copper Brass Bronze Copper-Silicon Alloys Monel Aluminum Shredded Lead	Teflon Kel-F Cotton-free Asbestos Graphite (Selected Types)	*
Fluorine and FLOX	Monel Aluminum Stainless Steel 304L 347 Copper Brass	None	None
Liquid Hydrogen	Stainless Steel 300 Series Austenitic Copper Bronze Brass Monel Aluminum	Dacron Teflon Kel-F Nylon Nylon Films Asbestos Impregnated with Teflon	*

*See note on title page.
For the proper lubricants to be used in this system, check the appropriate process specification and/or specification drawing.

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STORABLE OXIDIZERS

MATERIAL	METALS	NON-METALS	LUBRICANTS
Nitrogen Tetroxide	Carbon Steels Aluminum Stainless Steel Nickel Inconel	Ceramic (acid-resistant) Pyrex Glass Teflon Kel-F Asbestos (Cotton-Free)	*
Hydrogen Peroxide	Aluminum 1060 1260 1360 5254 5652 Stainless Steel 304 304ELC 309 310 316 316ELC 317 321 347	Teflon Kel-F	*
Inhibited Red Fuming Nitric Acid	Aluminum 1060 EC 1100 3003 3004 6061 5052 5154 Stainless Steel 347 19-9DL 19-9DX 304ELC 321 303 316	Kel-F Teflon Polyethylene	*

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STORABLE OXIDIZERS (CONTINUED)

MATERIAL	METALS	NON-METALS	LUBRICANTS
Chlorine Trifluoride	Stainless Steel 18-8 Copper Silver-solder Brass Steel Magnesium Aluminum Monel Nickel	Neoprene Pyrex Glass	None

STORABLE FUELS

MATERIAL	METALS	NON-METALS	LUBRICANTS
Hydrazine	Aluminum 2S & 3S Stainless Steel 303 304 321 347 Nickel	Polyethylene Teflon Kel-F Unplasticized	*
Monomethylhydrazine	Stainless Steel 304 307 Aluminum 3003 5052 5154 1060 6061 Durimet 20	Polyethylene Teflon Kel-F Unplasticized	*
Unsymmetrical-Dimethylhydrazine	Low Carbon Steels Aluminum Stainless Steel 300 Series	Teflon Kel-F Butyl Rubber JM-76	*
Hydyne	Stainless Steels Nickel Monel Aluminum 2S & 52S-0	Teflon Polyethylene	*

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STORABLE FUELS (CONTINUED)

MATERIAL	METALS	NON-METALS	LUBRICANTS
RP-1	Most Metals Avoid: Lead Copper Brass Zinc	Neoprene Teflon Kel-F Buna-N Synthetics	*
Ethyl Alcohol	Steel	Polyvinyl chloride Neoprene Rubber Kel-F Teflon Polyethylene Asbestos Gasket Material	*

PYROPHORIC FUELS

MATERIAL	METALS	NON-METALS	LUBRICANTS
Pentaborane	Aluminum 5052-S 6061-T6 7075-T6 2024-T3 3003-H14 356-T6 Stainless Steel 18-8 Low Carbon Steel K-Monel Monel M-8330-B Nickel Nichrome "V" Magnesium Fed QQ-M44A Fed QQ-M-56-A263 Titanium C-130AM C-110AM Copper Brass Hastelloy	Kel-F Kel-F-5500 Teflon Fluorosilicone Rubbers Fluoroflex "T" Glass Viton "A" & "B" Dry Asbestos Garlock 230 Carbon	*

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PYROPHORIC FUELS (CONTINUED)

MATERIAL	METALS	NON-METALS	LUBRICANTS
Triethylaluminum Triethylboron Triethylaluminum-boron	Stainless Steel Copper Iron	Glass Teflon Kel-F	*

SOLVENTS

MATERIAL	METALS	NON-METALS	LUBRICANTS
Acetone Freons Trichloroethylene	ANY NON-ORGANIC MATERIALS		

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APPENDIX D

Compilation of Facts

Concerning

Protective Clothing

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CRYOGENICS

	LOX	LN_2	LHe
Head Protection	Hard Hat	Hard Hat	Hard Hat
Face Protection	Face Shield*	Face Shield*	Face Shield*
Body Protection	Cotton Work Clothes and Apron	Cotton Work Clothes and Apron	Cotton Work Clothes and Apron
Hand Protection	Asbestos Gloves	Asbestos Gloves	Asbestos Gloves
Foot Protection	Nail-Free Work Shoes	Nail-Free Work Shoes	Nail-Free Work Shoes
Respiratory Equipment	None Required	Required When Suffocation Hazard Is Present	Required When Suffocation Hazard Is Present

	FLUORINE	FLOX	HYDROGEN
Head Protection	Gra-Lite Hood**	Gra-Lite Hood**	Hard Hat
Face Protection	Gra-Lite Hood**	Gra-Lite Hood**	Face Shield*
Body Protection	Gra-Lite Suit**	Gra-Lite Suit**	Cotton Work Clothes and Apron; Flash Suit
Hand Protection	Neoprene Gloves	Neoprene Gloves	Asbestos Gloves
Foot Protection	Neoprene Boots	Neoprene Boots	Nail-Free Work Shoes
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When Suffocation Hazard Is Present

*Safety glasses must be used when face protectors are used.
**Armalon suits will replace Gra-Lite suits as they become available.

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STORABLE OXIDIZERS

	NTO	HYDROGEN PEROXIDE	IRFNA	CHLORINE TRIFLUORIDE
Head Protection	Gra-Lite Hood	Hard Hat	Gra-Lite Hood	Gra-Lite Hood**
Face Protection	Gra-Lite Hood	Face Shield*	Gra-Lite Hood	Gra-Lite Hood**
Body Protection	Gra-Lite Suit	Vinyl Apron	Gra-Lite Suit	Gra-Lite Suit**
Hand Protection	Vinyl-Coated Gloves	Vinyl-Coated Gloves	Vinyl-Coated Gloves	Neoprene Gloves
Foot Protection	Neoprene Boots	Neoprene Boots	Neoprene Boots	Neoprene Boots
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When Excessive Vapors Are Present	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded

*Safety glasses must be used when face protectors are used.
**Armalon suits will replace Gra-Lite suits as they become available.

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STORABLE FUELS

	HYDRAZINE	MMH	UDMH
Head Protection	Gra-Lite Hood	Gra-Lite Hood	Gra-Lite Hood
Face Protection	Gra-Lite Hood	Gra-Lite Hood	Gra-Lite Hood
Body Protection	Gra-Lite Suit	Gra-Lite Suit	Gra-Lite Suit
Hand Protection	Vinyl-Coated Gloves	Vinyl-Coated Gloves	Vinyl-Coated Gloves
Foot Protection	Neoprene Boots	Neoprene Boots	Neoprene Boots
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded

	HYDINE	RP-1	ETHYL ALCOHOL
Head Protection	Gra-Lite Hood	Hard Hat	Hard Hat
Face Protection	Gra-Lite Hood	Face Shield*	Face Shield*
Body Protection	Gra-Lite Suit	Cotton Work Clothes	Cotton Work Clothes
Hand Protection	Vinyl-Coated Gloves	Neoprene Gloves	Vinyl-Coated Gloves
Foot Protection	Neoprene Boots	Nail-Free Work Shoes	Nail-Free Work Shoes
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded

*Safety glasses must be used when face protectors are used.

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PYROPHORIC FUELS

	PENTABORANE	TEA	TEB	TEAB
Head Protection	Gra-Lite Hood	Hard Hat	Hard Hat	Hard Hat
Face Protection	Gra-Lite Hood	Face Shield*	Face Shield*	Face Shield*
Body Protection	Gra-Lite Suit	Open-Back Jacket or Apron	Open-Back Jacket or Apron	Open-Back Jacket or Apron
Hand Protection	Vinyl-Coated Gloves	Asbestos Gloves	Asbestos Gloves	Asbestos Gloves
Foot Protection	Neoprene Boots	Heavy Rubber Boots	Heavy Rubber Boots	Heavy Rubber Boots
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded

*Safety glasses must be used when face protectors are used.

SOLVENTS

	ACETONE	FREONS	TRICHLOROETHYLENE
Head Protection	Hard Hat	Hard Hat	Hard Hat
Face Protection	Face Shield*	Face Shield*	Face Shield*
Body Protection	Plastic Apron	Plastic Apron	Plastic Apron
Hand Protection	Neoprene Gloves	Neoprene Gloves	Neoprene Gloves
Foot Protection	Nail-Free Work Shoes	Nail-Free Work Shoes	Nail-Free Work Shoes
Respiratory Equipment	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded	Required When MAC Figure Is Exceeded

*Safety glasses must be used when face protectors are used.

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APPENDIX E

Compilation of Facts

Concerning

First Aid Treatment

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SUBJECT: Compilation of Facts Concerning First Aid Treatment

Appendix E

UNIT: Liquid Propellant Handling

FIELD: Propellants

ALL MATERIALS

CRYOGENS, STORABLE OXIDIZERS, STORABLE FUELS, PYROPHORIC FUELS, AND SOLVENTS

SKIN CONTACT:

Flush with large quantities of water for purposes of dilution, warming the affected area in the case of cryogens, or cooling it in the case of pyrophoric fuels, and generally washing off the area to remove the material.

EYE CONTACT:

Hold the eyes open and flush with water for a minimum period of fifteen (15) minutes to wash out the liquid.

INHALATION:

Remove the person from the contaminated area. Do not allow the person to walk; carry him.

INGESTION:

Summon medical help.

BREATHING STOPS:

Apply artificial respiration, or mouth-to-mouth resuscitation.

IN ALL CASES WHERE A PERSON REQUIRES FIRST AID, SUMMON MEDICAL HELP.

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APPENDIX F

Compilation of Facts

Concerning

Fire Control

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CRYOGENICS

1½ space

	LOX	LN_2	LHe
Water Dilution and Cooling			
Stream	NO	NOT	NOT
Spray	NO	FLAMMABLE	FLAMMABLE
Fog	YES		
Suffocation Method			
CO_2	NO		
Dry Chemical	NO		
Foam	NO		

1½ space

	FLUORINE	FLOX	HYDROGEN
Water Dilution and Cooling			
Stream	NO	NO	YES
Spray	NO	NO	YES
Fog	Possibly*	Possibly*	YES
Suffocation Method			
CO_2	NO	NO	YES#
Dry Chemical	NO	NO	YES
Foam	NO	NO	NO (Will Freeze)

1½ space

*Fluorine reacts with water; therefore, it cannot be used to put out a fluorine-fed fire, but a controlled fog stream can substantially reduce toxic effluent by controlled reaction.

#CO_2 is not as effective as water because of the high temperatures involved.

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STORABLE OXIDIZERS

	NTO	HYDROGEN PEROXIDE	IRFNA	CHLORINE TRIFLUORIDE
Water Dilution and Cooling				
Stream	YES	YES+	YES++	NO
Spray	YES	YES+	YES++	NO
Fog	YES	YES	YES	Possibly*
Suffocation Method				
CO_2	NO	NO	NO	NO
Dry Chemical	NO	NO	NO	NO**
Foam	NO	NO	NO	NO

+Large amounts of water can effectively dilute peroxide.

++In an enclosed area, large amounts of water on IRFNA can cause an increase in vapor pressure.

*Chlorine trifluoride reacts with water; therefore, it cannot be used to put out a fire, but a controlled fog can substantially reduce toxic effluent by controlled reaction.

**Dry chemicals can be used to decontaminate spills.

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STORABLE FUELS

	HYDRAZINE	MMH	UDMH
Water Dilution and Cooling			
Stream	YES	YES	YES
Spray	YES	YES	YES
Fog	YES	YES	YES
Suffocation Method			
CO_2	YES	YES	YES
Dry Chemical	YES	YES	YES
Foam	YES*	YES*	YES*

	HYDYNE	RP-1	ETHYL ALCOHOL
Water Dilution and Cooling			
Stream	YES	NO	YES
Spray	YES	NO	YES
Fog	YES	YES	YES
Suffocation Method			
CO_2	YES	YES	YES
Dry Chemical	YES	YES	YES
Foam	YES*	YES	NO (Dissolves)

*Foam tends to break down rapidly due to the high temperature of hydrazine-fed fires. CO_2 is effective in most cases involving small fires, especially for protection of personnel.

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PYROPHORIC FUELS

	PENTABORANE	TEA	TEB	TEAB
Water Dilution and Cooling				
Stream	NO	NO	NO	NO
Spray	NO	NO	NO	NO
Fog	Possibly*	Possibly*	Possibly*	Possibly*
Suffocation Method				
CO_2	YES+	YES+	YES+	YES+
Dry Chemical	YES+	YES+	YES+	YES+
Foam	YES++	YES++	YES++	YES++

Correct

*Pyrophoric fuels react violently with water; therefore, they cannot be used to put out a fire, but a controlled fog can be used to burn up the fuel faster, while providing cooling for the surrounding area.

+CO_2, dry chemical, and foam are effective as long as they cover the fire; once removed, the fire may reignite.

++Foam and water deluge are the most effective control.

SOLVENTS

	ACETONE	FREONS	TRICHLOROETHYLENE
Water Dilution and Cooling			
Stream	NO	*	NO
Spray	NO	*	NO
Fog	YES	*	YES
Suffocation Method			
CO_2	YES	*	YES
Dry Chemical	YES	*	YES
Foam	YES	*	YES

*At the present time, Freon solvents are considered to be non-flammable.

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SUBJECT: Nitrogen Tetroxide (NTO) INFORMATION Sheet

UNIT: Liquid Propellant Handling B-1

FIELD: Propellants Page 1 of 3 pages

DEFINITION:

Nitrogen tetroxide is used as a storable oxidizer which contains 70% oxygen per unit volume.

ESSENTIAL FACTS, IDEAS, AND PROCEDURES:

Nitrogen Tetroxide

Nitrogen tetroxide (NTO) goes by several names, including dinitrogen tetroxide, nitrogen peroxide, and liquid dioxide. It is a heavy, brown liquid, at ordinary temperatures, containing about 30% N_2 and 70% O_2. In comparison to liquid oxygen, with a common fuel, it offers a slightly lower specific impulse. If the bulk density is used in the comparison, nitrogen tetroxide has a slightly higher impulse/cu. ft.

Nitrogen tetroxide is storable for long periods of time if kept free of contaminants. It has the advantage of being almost instantaneously hypergolic with most fuels. The use of NTO with a particular fuel, which forms a hypergolic mixture, eliminates the need for a complete, heavy, start system.

Properties

Because of moderate freezing (11.85°F) and boiling points (70.1°F), nitrogen tetroxide is easily stored at normal ambient temperature in the Southern California area. Even at temperatures of 100°F, the vapor pressure is only 16 psig. Nitrogen tetroxide has a sharp, pungent odor, but this odor does not give sufficient warning of the presence of toxic vapors. The vapors are extremely toxic. The MAC for a continuous 8-hour day is 5 ppm by volume.

Normally a reddish brown liquid, the gas varies in color from brown to yellow when mixed with air.

Pure nitrogen tetroxide is stable against mechanical shock. It is hypergolic with many fuels, and may induce spontaneous ignition if brought in contact with paper, cloth, wood, etc.

Free of water, and in its pure form, nitrogen tetroxide is only mildly corrosive. If storage containers are not sealed, moisture may be absorbed by the tetroxide, with the formation of very corrosive nitric acid resulting.

Protective Clothing and Equipment

Because of the oxidizing ability and extreme toxicity of nitrogen tetroxide, personnel must be fully protected from contact

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with it. This includes the use of Gra-Lite hoods, vinyl-coated gloves, neoprene boots, and, when in concentrations above 2%, a Scott Air-Pak. During most transfer operations, between shipping containers and the storage container, a cannister type of respiratory equipment will suffice. Under all circumstances, one individual must stand by in equipment suited for maximum hazardous conditions.

First Aid

Contamination through spillage of nitrogen tetroxide warrants immediate attention. The affected area must be flushed with water for at least 15 minutes. The use of small amounts of water causes the formation of concentrated nitric acid, and results in serious acid burns. Clothing should be removed and washed thoroughly.

Inhalation of the vapors forms nitric acid in the respiratory tract with pulmonary irritation resulting, which may then result in pulmonary edema, laryngitis, bronchitis, and pneumonitus. Effects from exposure to the vapors may be delayed for a period of several hours. Injury occurs during the formation of nitrates and nitrites in the neutralization process. Any exposure, whether by inhalation or direct contact, needs immediate medical treatment.

Fire Protection

Fires fed by nitrogen tetroxide will continue to burn until all of the oxidizer has been consumed or used up in some manner. A water fog is most effective in combating this type of fire. In addition to cooling the flame, the water dilutes the tetroxide to a weakened acid solution. Care must be taken to use large quantities of water to prevent acid corrosion.

Storage and Handling

Nitrogen tetroxide, until recently, was shipped entirely in one-ton cylinders. Because of the extent to which the storable propellant program has grown, shipping by tanker truck has become more practical.

The cylinders are constructed of mild steel capable of withstanding moderate pressures. The tetroxide may be removed from the cylinders by pressurization. Tanker trucks may be emptied by pumping or pressurization.

All storage containers must be sealed to prevent the escape of toxic vapors and the entrance of moisture into them when not in use. Even though precautions are taken, the containers are subject to corrosive action.

All storage areas should be free of flammable materials, and be provided with good ventilation. A graded storage area should be

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provided to facilitate easy drainage after flooding the area. An abundant and accessible water supply is necessary in such a storage area.

Compatible Materials

The following materials and lubricants have been found to be compatible with nitrogen tetroxide:

Metals (When NO_2 moisture is 0.1% or less)

Carbon Steels

Aluminum
Stainless Steels
Nickel
Inconel

Non-Metals

Ceramic (acid-resistant)
Pyrex Glass
Teflon
Kel-F
Asbestos (cotton-free)

Lubricants

See note on title page.

For the proper lubricants to be used in this system, check the appropriate process specifications and/or specification drawings.

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INTERNAL LETTER

NORTH AMERICAN AVIATION, INC.

		DATE	13 August 1964
TO ADDRESS	J. Blake D/056, Zone 12 Rocketdyne-SSFL	FROM ADDRESS	E. Roddy D/051, Zone 12 Rocketdyne-SSFL
		PHONE	5273 or 5272

SUBJECT REVIEW OF OFF-STAND PROPELLANT SAMPLING

The Industrial Hygiene and Safety Section, D/051 has conducted a survey of the off-stand storage vessel sampling operations performed periodically by D/056. This survey was requested by D/056 to:

(1) Detect any potential hazards incident to the sampling operation,

(2) Evaluate the control measures employed to protect personnel, and

(3) Make recommendations to improve existing controls and/or initiate additional controls.

Safety implications pertinent to sampling methods, sample containers, and the handling and transporting of samples were given consideration.

Samples are drawn from ports on the storage vessel. Generally, samples are obtained by one of two methods. Gravity flowing a sample from a tap on the storage vessel into a sample container or passing the contents of the vessel through the sampler and trapping a portion. The portion passing through the sampler can be expelled to atmosphere or returned to the storage vessel depending upon conditions. Toxicity, volatility, and stability are some of the factors that will influence the choice of the sampling method and the sample container.

The samples are collected in several types of containers. Those most often used are:

(1) Glass bottles.

(2) Polyethylene bottles.

(3) 1800 psi S.S. sausage bombs.

(4) 3000 psi S.S. one liter bombs.

(5) 4.4 liter S.S. Cosmodyne sampler (675 psi).

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Following is a list of materials routinely sampled from the off-stand storage vessels and the type of containers generally used:

(1) Hydrazine fuels - glass or polyethylene bottle or one liter bomb.

(2) Nitrogen tetroxide and fuming nitric acids - glass or polyethylene bottle or one liter bomb.

(3) Liquid oxygen - one liter bomb or 4.4 liter sampler.

(4) Hydrocarbon fuel (RP-1) - glass or polyethylene bottle.

(5) Pressurizing gases, inert - sausage or one liter bomb.

(6) Liquid nitrogen - sausage or one liter bomb.

(7) Gaseous hydrogen and oxygen - sausage or one liter bomb.

(8) Trichloroethylene - glass or polyethylene bottle.

(9) Liquid hydrogen - no approved method at the present time. An attempt is being made to adapt the 4.4 liter sampler to LH_2 sampling.

(10) Moisture content of gases - Alnor Dew Pointer or Robbins Aviation Sampler.

Many problems arise trying to obtain a representative sample of a toxic or cryogenic material while keeping personnel exposure to hazards to a minimum. Some of the items noted during the survey were:

(1) Some of the storage vessels have no provision for taking a sample.

(2) Some storage vessels have sample ports located so they are not easily accessible.

(3) Some sample systems are poorly constructed and have no pressure relieving capability.

(4) Some times, sample units are connected into systems where the pressure exceeds the maximum rating of the sampler.

(5) Some sample units have components that are rated lower than the maximum pressure rating of the unit.

(6) Toxic and flammable vapors released from the sampler are not always adequately controlled.

The following recommendations are aimed at minimizing the hazard to personnel while sampling toxic, corrosive, and flammable materials and to facilitate sampling operations:

(1) Include provisions for sampling in the design of all off-stand storage vessels; the design should be reviewed by D/056 and D/051.

(2) Standardize the sampling systems to conform as near as practical with the system shown in Enclosure (1).

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(3) Install sampling systems on all storage vessels that do not have them as soon as it is feasible.

(4) Revise existing systems to conform with Enclosure (1) wherever it is practical.

(5) Locate sample ports where they are easily accessible; relocate existing ports that are difficult to reach.

(6) Provide all sample systems with adequate relieving capability.

(7) Prohibit connecting samplers into systems where the pressure exceeds the maximum pressure rating of the sampler without an appropriate regulator.

(8) Prohibit the use of samplers on systems where the pressure exceeds the lowest maximum rating of any of the sampling components.

(9) Sampling systems should be constructed so that significant concentrations of toxic and/or flammable vapors are not released in an uncontrolled manner.

(10) Write and maintain standing operating procedures for all sampling operations including transportation of the samples; have the procedures reviewed by Industrial Hygiene and Safety, D/051 and the Fire Department, D/052.

(11) Place breakable sample containers in an appropriate outer container immediately after sampling.

(12) Have samples packaged so that they will be able to withstand conditions normally incident to handling and transportation (if this is impractical, then assign the responsibility for insuring the safe arrival of the sample at its destination to someone who has adequate knowledge of the potential hazards incident to handling and transporting the sample).

(13) Eliminate open system sampling of toxic materials, where this is impractical and have Industrial Hygiene and Safety investigate the specific operation to determine the extent of the hazard and recommend control measures if needed.

In the event that specific problems arise pertinent to the hazards involved in obtaining, handling, and transporting samples, contact Industrial Hygiene and Safety, D/051 and the Fire Department, D/052.

Two specific problems were encountered during the survey. One pertaining to sampling liquid hydrogen. The Cosmodyne 4.4 liter sampler has been used to sample LH_2 and the excess hydrogen vented off to atmosphere through a six-foot portable vent line. The Industrial Hygiene and Safety Section, D/051 does not approve of the uncontrolled release of GH_2 in this manner and will require more positive control of the vented hydrogen. The other problem was the apparent release of excessive vapors while using the one liter bomb to sample NTO. In this instance, the principle appears sound and refinement of the system should eliminate the problem.

Earle Roddy

E. Roddy
Industrial Hygiene & Safety
Representative

ER:lkk

Enclosures (1)

BNA08768411

HDMSP001794098

Internal Letter

Rockwell International

Date: 10 April 1986

No: FL346-83-013 (Revised)
27876/00926

TO: (Name, Organization, Internal Address)

Engineers, Supervisor,
Leadmen, Mechanics
D/598-346, 055-SS11

FROM: (Name, Organization, Internal Address, Phone)

S. Fischler
Rocketdyne - SSFL
D/598-346, 055-SS11
5087

Subject: Handling and Shipping of Hardware or Equipment Exposed to Storable Propellants

Ref.: Field Lab Procedures #108 and #113 (copies attached)

ALL D/598-346 personnel are required to be familiar with the requirements of Field Lab Procedures 108 and 113 regarding the handling of hardware or equipment exposed to storable propellants.

Procedures or EWR's specifying decontamination or flushing processes to be utilized on hardware shall include steps detailing verification of the decontamination procedure by use of the MSA tube and attaching the yellow "Caution" tags (Form 614-C-2).

NO hardware is to be shipped from APTF, STL-IV, SPA, ECL or the NAKA/Happy Valley complex unless: 1) the hardware has been decontaminated in accordance with approved procedure or EWR; 2) the hardware has been "sniffed" to verify the absence of contaminants which may be dangerous if improperly handled; and 3) the yellow "Caution" tags (Form 614-C-2) are attached to the hardware. Equipment shipped to the Equipment or Instrumentation Laboratories does require the MSA "sniff" test, and aspiration is not a substitute for decontamination.

Effective immediately, ALL operating procedures or EWR's must call out these specific steps and shall include sign-offs for each of these steps.

S. Fischler, Manager
Chemical & Advanced Component Test

SF:jr

Attachments: Page 1 of FLP #108, and Page 2 of FLP #113

Form 131-R Rev. 3-76

BNA08768412

HDMSP001794099

SUBJECT: DECONTAMINATION, INERTING AND PURIFICATION REQUIREMENTS

1.0 SCOPE

This procedure establishes the requirement for the preparation of decontamination, inerting and purification procedures appropriate to the operations being conducted. These procedures are not to apply to test hardware as these items must be covered by specific hardware specifications and procedures.

2.0 DEFINITIONS

2.1 Decontamination as used herein pertains to those steps required to render a part or system safe to be approached or handled without protective measures, equipment or clothing.

2.2 Inerting is the process of diluting a combustible gas or vapor with an inert gas or vapor to make the contents nonflammable or nonexplosive.

2.3 Purification is the process of eliminating fluids introduced in the decontamination and/or inerting process in preparation for filling the system with the service fluid. Purification usually involves displacing air or nitrogen with a gas that is compatible with the service fluid.

3.0 REQUIREMENTS

3.1 Each SSFL Unit having responsibility for decontamination, purification and inerting of parts or systems shall prepare procedures covering the necessary operations to ensure that such operations are properly performed.

3.2 Copies of these procedures shall be maintained in the Area Operating Instruction Manual.

3.3 Decontamination is required if the yellow warning tags (Ref. FL Procedure 113) are to be removed or if a previously contaminated part is being shipped or otherwise handled as being contaminant free.

3.4 Decontamination is not required if a yellow tagged item is to be returned to service.

3.5 The procedures outlined in Appendix A are general in nature and may be used in whole or in part or as a guide in developing area procedures which are specific in nature for the equipment and service involved.

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USE OF WARNING TAGS AND STREAMERS

3.1.2 During facility operations, it is often necessary to place an item in an energized position and leave the console unattended. In the event this is necessary, the appropriate console switches shall be red warning tagged as per 3.1.1. Before red warning tagging, the operator shall obtain verification from the responsible engineer that the integrity of the system will not be violated, and that the item being energized is capable of continuous duty service within the time element involved.

3.2 YELLOW "CAUTION" TAGS (Form 614-C-2)

3.2.1 All items which are potentially contaminated with a material that is hazardous to personnel or equipment, but which are safe for shipment, shall be tagged with a yellow "CAUTION" tag (Form 614-C-2).

3.2.2 The person responsible for initiating shipment shall fill out the top part of the card (contaminating material, test site removed from, date removed). Each subsequent recipient of tagged items who disassembles and disperses its components shall be responsible for attaching additional tags to each potentially contaminated component.

3.2.3 The tag shall be securely attached in a conspicuous location. Large assemblies should have additional tags attached.

3.2.4 All items to be scrapped, returned to storage or to open stock, shall be decontaminated. After an item has been decontaminated, the bottom part of the tag shall be filled out by the person responsible for decontamination (person who performed decontamination, location, and date).

3.2.5 The tag shall remain attached to decontaminated items returned to storage or open stock to assist in determining subsequent cleaning operations. The tag shall also remain attached to decontaminated items to be scrapped to assist in determining proper disposal procedures. The tag shall be removed and discarded when an item is cleaned and/or returned to service.

3.3 RED WARNING STREAMERS. Red warning streamers shall be used to indicate a disabling item installed into a system when the item will prevent normal operation of the system or create a hazard to operation.

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Need No. 402

1. ID Number: 402

2. Title: Personal Dosimeter Badge for Monitoring Exposure to Hydrazine Fuel Vapors at Rocket Launch Sites

3. Pillar Supported: Occupational Health

4. Priority: High

5. Media: Air

6. Contaminant(s):

- Hydrazine
- Monomethylhydrazine (MMH)
- Unsymmetrical Dimethylhydrazine (UDMH)

7. Key Policy or Regulatory Driver:

- AFOSH Std 48-8 Controlling Exposures to Hazardous Materials
- EWR 127-1 provides requirements for hydrazine-fuel leak detection and the threshold limit value monitoring for fuel vapors in air at Cape Canaveral Air Station (CCAS) (East Range) and Vandenberg AFB (VAFB) (West Range).

8. Need Description: Shirt-pocket-size personal dosimeter badges need to be developed for monitoring worker exposure to hydrazine rocket fuels in air. The Air Force uses hydrazine and MMH in satellites and Aerozine-50 (50% UDMH, 50% hydrazine) in Titan and Delta launch vehicles. The fuels are highly toxic and are listed as "A2 - suspected human carcinogens" by the American Conference of Governmental Industrial Hygienists (ACGIH). No commercial dosimeter can monitor hydrazine-fuel vapors at ACGIH's recently adopted (May 1995) threshold limit value (TLV) of 10 ppb, as an eight-hour time weighted average. Since most hydrazine-fuel exposures are short in duration, a dosimeter is also needed to ensure that the excursion exposure limit, 30 ppb as a 30 minute time weighted average, is not exceeded. In addition, the hydrazines have "skin" notations, which indicate that a significant part of the overall exposure can take place by the cutaneous route, including the mucous membranes, eyes, and skin. this portion of the actual dose cannot be measured except through biological monitoring. Therefore, the need to accurately characterize the potential dose by inhalation is crucial, as it is potentially only part of the total dose. By AFOSH Standard 48-8, these ACGIH-adopted TLVs have automatically become AFOSH requirements. The ACGIH/AFOSH adopted 10 ppb TLVs are up to 50 times lower than the previous hydrazine-fuel TLVs. In an Aerozine-50 leak, UDMH detection is of primary concern because of its high volatility and its ability to form N-nitrosdimethylamine, a highly carcinogenic air oxidation product. UDMH detectors are used solely by the Air Force. The lowering of the permissible exposure levels of hydrazines will soon affect numerous Air Force space programs because of widespread use of hydrazine fuels. There will likely be an increased need for launch personnel to wear self-contained respirators, resulting in lower operational efficiencies and increased costs. The availability of reliable personal dosimeters could provide cost savings by determining when respirators and other personal protective equipment are no longer needed. Reliable dosimeters are needed to protect the health of launch site workers and to document allowable personal exposure conditions to protect the government and contractors from future litigation. (It should be noted that the newly-adopted allowable exposure levels for hydrazine fuels, which have been described, require both dosimetry and real-time concentration monitoring. This need statement responds to the need for a dosimeter only. Need statement #413 responds to the separate need for a real-time concentration monitor.)

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Current System Description: No cost-effective commercial detectors are available that can reliably detect hydrazines at the ACGIH/AFOSH adopted 10 ppb TLVs. Moreover, no commercial dosimeters are available that can monitor hydrazine fuels and provide an alarm to the user at the 30 ppb, 30 minute excursion limit, or at one-half the TLV dose levels, as is desired. Several vendors produce fixed-point area detectors and portable detectors that can monitor hydrazine fuels at one-half their previous TLVs (i.e. at one-half of 100, 200, and 500 ppb for hydrazine, MMH, and UDMH, respectively). The operating principle of these detectors is generally colorimetry or electrochemistry. Extensive testing at the Naval Research Laboratory and NASA KSC's Toxic Vapor detection Laboratory using calibrated hydrazine-fuel/airstreams has shown (notwithstanding manufacturer claims) that the lower detection limits of the commercial fixed-point electrochemical and colorimetric detectors, even under controlled laboratory conditions and in the absence of interferences, are generally about 20 and 25 ppb, respectively. the detection limits for portable versions of these instruments are generally about 40-50 ppb. The detection limits of these instruments in the field are even higher. One vendor has markedly increased the sample flow rate through their electrochemical detector so that it can detect 10 ppb levels of hydrazines. However, the increased flow rates have given rise to limited detector lifetimes and the need for too frequent maintenance.

Waste/Volume/Other Environmental Concerns: At CCAS and Kennedy Space Center (KSC), area and portable monitors are used at rocket launch and payload processing facilities. The rockets and their launch facilities are: Delta, Space Launch Complex (SLC) #17; Atlas, SLC #36; Titan IV, SLC #40 and #41; and Shuttle, SLC #39 Pads A and B. The area monitors (including leak detectors) are used to monitor fuel vapors at SLC #17, 36, 39 A and B, 40, 41, the DSCS Processing Facility, the NAVSTAR Processing Facility, and the Spacecraft Processing and Integration Facility. Portable monitors (including personal monitors) are used at SLCs #17, 39 A and B, 40, 41, Fuel Storage Area #1, Wiltech analytical laboratory, and at other locations as needed. At VAFB, area and portable monitors are used at SLC #2, SLC #3, and SLC #4W and #4E in Delta, Atlas, and Titan launch operations. Each Titan IV launch vehicle uses 150,000 lbs of Aerozine-50, the Delta stage 2 uses 4,700 lbs of Aerozine-50, the Shuttle orbiter OMS and RCS engines use 12,500 lbs of MMH, while payloads and Atlas use small, variable quantities of MMH and hydrazine.

Current Cost of Process: Current colorimetric- or electrochemical-based area monitors cost between about $4K and $8.5K per unit, while the corresponding hand-held instruments generally cost between $2.5K and $4.5K per unit. It is estimated that 200 to 300 hydrazine-fuel detection instruments are used at each launch range (CCAS, KSC, and VAFB). Instrument lifetimes are about 3 years. Instrument costs for all ranges probably thus average $1.5 million per year. Since the TLVs have been lowered, more sensitive, reliable monitors are required. If reliable monitors are not available, the costs associated with operational delays prior to launch due to false positive alarms could be as high as a few hundred thousand dollars a year. The costs associated with each day of delay of a Titan IV launch is $2 million ($80K/hour). Possible unfavorable legal judgments against the government due to adverse health impact to launch-site personnel unknowingly exposed to hazardous levels of hydrazines could be even higher (tens of millions of dollars).

Extent of the Problem: The problem of not being able to detect hydrazine fuels at the ACGIH/AFOSH adopted 10 ppb TLVs and monitor the fuels at the 30 ppb, 30 minute excursion limit could impact Air Force launch activities at Vandenberg AFB, Cape Canaveral Air Station, and Kennedy Space Center. ERR 127-1 provides requirements for fuel leak detection and the monitoring of the ambient atmosphere at CCAS. Analogous requirements also exist at KSC and VAFB. Similar requirements exist for monitoring hydrazine at F-16 aircraft servicing facilities.

Standards/Specifications Impacted: AFOSH Standard 48-8 and other fuel detection standards.

Known R&D Efforts: POC: Lt. Amon Martin, Chief, Launch Project Support, SMC/CLNE, COMM (310) 363-2301, DSN 833-2301, COMM FAX (310) 363-3429, FAX-DSN 833-3429. "Development of a personal alarm, conductive-polymer, hydrazine-fuel exposure sensor:" A promising dosimeter badge has been developed by Spectra Sciences, Inc. (SSI) and SMC-designated SBIR Phase I and II funding. Tests, performed over a range of temperature and humidity conditions present at launch sites, show that the conductive-polymer sensors can provide minimal detectable doses of 2 ppb-hours and saturation doses of greater than 150 ppb-hours for UDMH and hydrazine vapors. Thus, sensors can readily monitor fuels at the desired 15 and 40 ppb-hour dose levels. Funding is needed to further develop this dosimeter during FY96. In this

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ppb-hour dose levels. Funding is needed to further develop this dosimeter during FY96. In this effort, SSI will develop (a) a compact badge-housing for the sensor and associated alarm circuitry, (b) a reliable sensor reader for monitoring accumulated doses at the start and end of each work shifts, (c) an easily used data analysis and display software package, (d) methods for reproducible results. The dosimeter badge system will then be extensively field tested at CCAS. ATSDR Toxicologic Profile contains several leads.
Outside Needs: POC: Ms. Sherry Duff, Chairperson Chemical Manufacturer's Hydrazine Coalition Olin Chemicals (203) 356-3166 Hydrazine producers and users (from large- to small-scale) will all require dosimeters able to monitor hydrazine, MMH, and UDMH vapor exposure at the desired 15 and 40 ppb-hour doses. CMA's Hydrazine Coalition is familiar with the personnel protection needs of these commercial organizations.

9. Urgency: 1997

Non-Compliance: If dosimeters are not developed for monitoring UDMH, MMH, and hydrazine at doses below the ACGIH adopted permissible exposure levels, then the Air Force will not be able to comply with AFOSH Standard 48-8 and the requirements governing hypergol vapor monitoring at CCAS, KSC, and VAFB (such as ERR 127-1 outlined in need description above). Without the required dosimeters, all launch site personnel may be required to wear self-contained respirators at all times in any location where fuel vapors could be present. It may be required that air samples be collected in fuel-storage or use areas and then analyzed at a laboratory by time-consuming wet chemical methods to verify sub-10 ppb fuel vapor levels before personnel may enter the area. These procedures would result in lower operational efficiencies, increased costs, and possible schedule delays. By not being able to comply with AFOSH monitoring requirements, the government and contractors may be burdened with routinely collected air samples and concomitant record keeping to document a safe workplace, as protection against future litigation. Estimates of costs associated with noncompliance are difficult to quantify, but could be tens of millions of dollars if launch delays or costly litigation results.

10. Alternative Options:

Current Method of Reducing the Problem: SMC/CL and SMC/ME have jointly funded research and development efforts on detectors and dosimeters designed to meet TLVs recently adopted by ACGIH/AFOSH. Over the past four years, $1M of SMC funds and $1.4M of SMC-designated SBIR funds have been provided to five different development efforts. Funding is now required to field test the dosimeter and to develop a brassboard dosimeter system.
Potential Solutions: Under SMC-originated SBIR Phase I and II funding, Spectral Sciences, Inc. has developed a shirt-pocket-size, conductive polymer-based personal dosimeter badge that can monitor worker exposure to hydrazine fuels at desired dose levels. This effort now requires additional funding to perform field tests on the breadboard version of the dosimeter and to allow development of a final, fully engineered brassboard design that is ready for commercialization.
Minimal Success Criteria: The development of a detector that reliably monitors hydrazine fuels (particularly UDMH) at levels below 10 ppb in air. The detector should be demonstrated at NASA's TVD lab or the Naval Research Lab to provide the following performance: (1) sufficient sensitivity to detect sub-10 ppb levels of UDMH (and if possible, hydrazine and MMH) with a +/- 20% accuracy. (2) a detection reproducibility at sub-10 ppb levels of +/- 20% (3) response and recovery times of less than five minutes to 90% and 10% respectively, of the full 10 ppb level upon step-function concentration changes between 0 and 10 ppb. (4) high specificity in discriminating against potential launch site interferences such as amines, ammonia, NO2, alcohols, and chlorinated solvents. (5) minimal temperature and humidity effects. (6) a minimum 30-day interval between calibration and (7) a one year shelf-life.

11. Contacts:

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